THE AMERICAN PHYSIOLOGICAL SOCIETY
Founded in 1887 for the purpose of promoting the increase of physiological knowledge and its utilization.

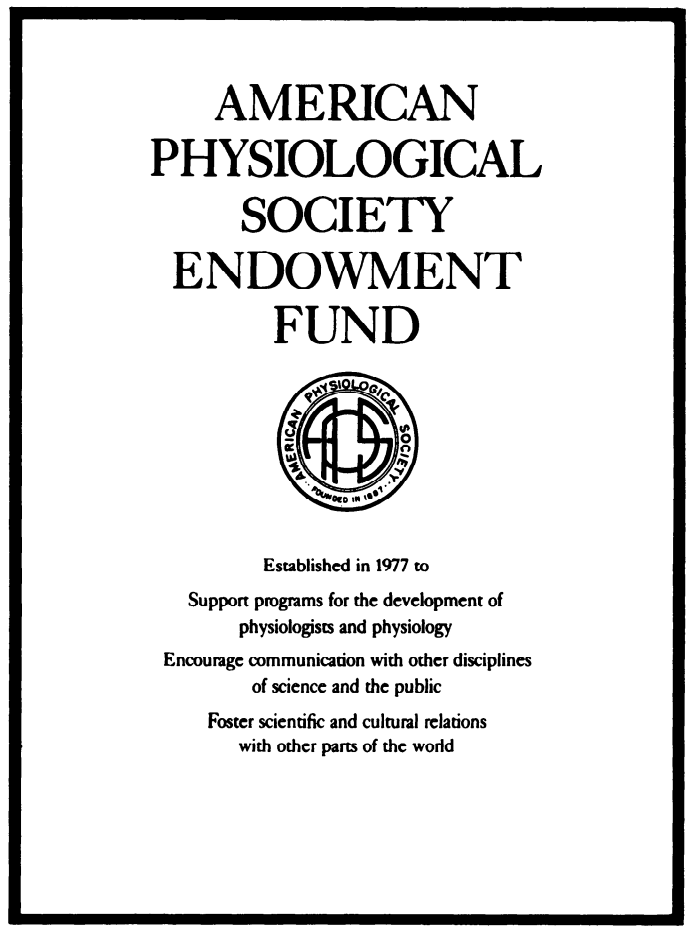
THE PHYSIOLOGIST is published bimonthly by the American Physiological Society at 9650 Rockville Pike, Bethesda, Maryland 20014. Address all correspondence to this address.

Subscriptions: Distributed with The Physiology Teacher to members as a part of their membership. Non-members and institutions, $12.00 per year in the United States; Canada, $12.50; Foreign and Postal Union, $13.00. The American Physiological Society assumes no responsibility for the statements and opinions advanced by contributors to THE PHYSIOLOGIST.

The Physiologist

A Publication for Physiologists and Physiology
Orr E. Reynolds, Editor

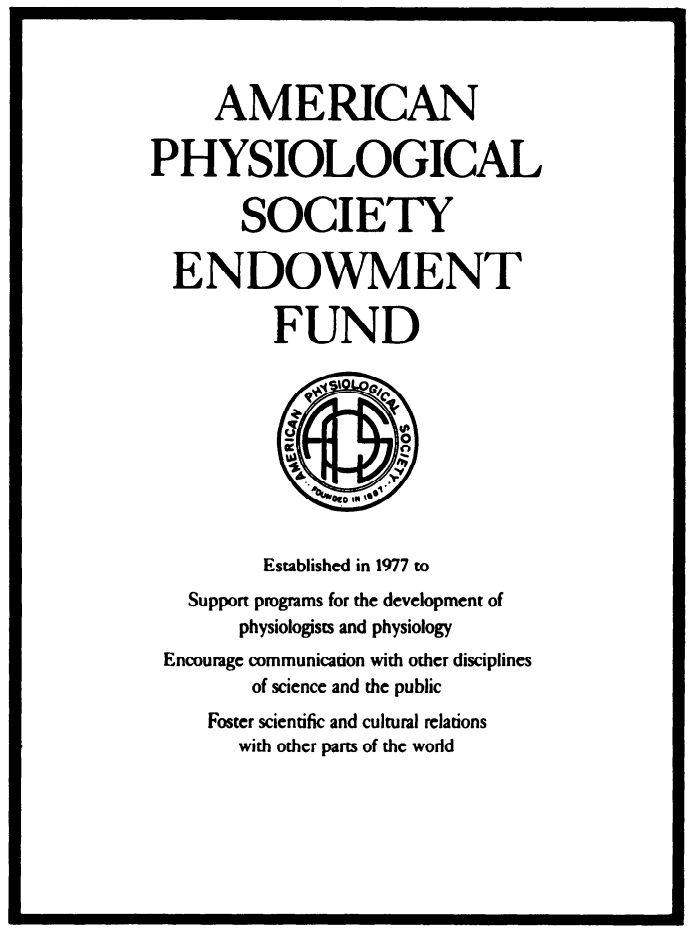
TABLE OF CONTENTS



The illustration above is a miniature reproduction of a bronze plaque being cast to hang in the APS Bethesda Office. Not shown are the individual shingles at the bottom of the plaque bearing the name of each living or deceased physiologist or other individual in whose memory the Endowment Fund is maintained. To date, the names of John F. Perkins, Jr. and Caroline tum-Suden have been so honored.

The APS Endowment Fund was established to encourage tax deductible contributions or bequests to the Society at any time and in any amount, for specific or general purposes. Upon request, the Society will provide to a donor or institution contributing a memorial gift a replica of the plaque bearing the name of the individual living or deceased in whose honor the gift was made. The family of, or the individual being honored by a donation to the fund will be advised formally of the donors name, unless the contributor specifically requests that the donation be anonymous.

Donations to the APS Endowment Fund or queries should be addressed to the fund at 9650 Rockville Pike, Bethesda, Maryland 20014.



The illustration above is a miniature reproduction of a bronze plaque being cast to hang in the APS Bethesda Office. Not shown are the individual shingles at the bottom of the plaque bearing the name of each living or deceased physiologist or other individual in whose memory the Endowment Fund is maintained. To date, the names of John F. Perkins, Jr. and Caroline tum-Suden have been so honored.

The APS Endowment Fund was established to encourage tax deductible contributions or bequests to the Society at any time and in any amount, for specific or general purposes. Upon request, the Society will provide to a donor or institution contributing a memorial gift a replica of the plaque bearing the name of the individual living or deceased in whose honor the gift was made. The family of, or the individual being honored by a donation to the fund will be advised formally of the donors name, unless the contributor specifically requests that the donation be anonymous.

Donations to the APS Endowment Fund or queries should be addressed to the fund at 9650 Rockville Pike, Bethesda, Maryland 20014.

AMERICAN PHYSIOLOGICAL SOCIETY
121st BUSINESS MEETING

TIME: 4:30 p.m., Sunday, April 8, 1979
PLACE: Fairmont Hotel, International Ballroom

I. CALL TO ORDER

Dr. David F. Bohr, President, called the meeting to order and welcomed the members to the 121st Business Meeting. The Ballot for Election of New Members, Proposed Amendments to the Bylaws, and a Statement of President Carter's budget for FY80 were distributed.

II. REPORT ON MEMBERSHIP

Dr. Ernst Knobil, President-Elect, reported on the membership status and deaths since the last meeting.

A. Membership Status

The membership in the Society continues to grow. In the last report, there were 5,267 members. Since then, the Society membership has grown with a net increase of 147 bringing the total to 5,414. As of this date, there are 4,160 Regular members, 452 Retired members, 9 Honorary members, 638 Associate members, 34 Corresponding, and 121 Student members.

B. Deaths Reported Since Last Meeting

Dr. Knobil read the names of those members whose deaths have been reported since the previous meeting and asked the members to stand for a moment of silence in tribute to them. (page 5)

III. ELECTION OF MEMBERS

A. Appointment of Tellers

Dr. Bohr appointed Drs. Leonard Share, Arthur Vander, Carl Rothe, and Charles Seidel as Tellers and requested they collect the Ballots for Election of New Members.

B. Election of New Members

Dr. Bohr announced that all candidates on the Ballot for Election of New Members were elected. (page 5)

IV. ELECTION OF OFFICERS

Reporting the Election of Officers by mail ballot, Dr. Reynolds announced that the new President-Elect is Dr. Earl H. Wood, and the New Councilors are: Dr. Leon Farhi for a four-year term and Dr. Samuel McCann to complete Dr. Wood's term which expires in 1982. The total number of ballots cast were 1,525 for President-Elect and 1,433 for Councilor.

V. DAGGS AWARD

One of the pleasant duties of the President, announced Dr. Bohr, was the annual presentation of the Daggs Award. This Award is given by the Society to recognize distinguished service to the Science and the Society of Physiology in honor of Ray G. Daggs, who was Executive Secretary-Treasurer, 1956-1972. This year, the recipient is Dr. John R. Pappenheimer, George Higginson Professor of Physiology at the Harvard Medical School, and Dr. Bohr was delighted and honored to present the Award to him. (page 9)

VI. AMENDMENTS TO BYLAWS

Dr. John Cook, Chairman of the Membership Advisory Committee, in referring to the handout on the proposed amendments to the Bylaws dealing with Emeritus and Student memberships, announced that the proposed amendments appeared in the December 1978 issue of *The Physiologist*. As a result of a proposal submitted by a member of the Society, it was recommended that the designation of "Retired" member category be changed to "Emeritus" member.

Upon motion made, seconded and passed unanimously, it was resolved that Article III, Section 6, *Retired Members,* be amended by changing the name "Retired" Members to "Emeritus" Members.

The proposed amendment for Student membership resulted from a proposal to amend the Bylaws that was tabled at the 117th Business Meeting (April 1977). This Bylaw is intended to open Student membership to all predoctoral students, including undergraduates where appropriate, when such students are significantly engaged in physiological work and wish to become identified with the activities of the Society and its members.

Upon motion made, seconded and passed unanimously, it was resolved that Article III, Section 8. *Student Members* as follows:

> Any student who is actively engaged in physiological work as attested to by two Regular members of the Society and who is a resident of North America. No individual may remain in this category for more than five years, without reapplying.

VII. REPORTS

A. Finance Committee

The Finance Committee is composed of Arthur Guyton as Chairman, Daniel Tosteson and Robert Forster. Dr. Guyton reported that the Society has an annual income of a little over $2 million a year, most of which is for publications. One of the major purposes of the Society is publications and the other major function is the meetings. The publications income is $1.7 million, and next year, the income will be a little less. During the past two years, publications made a considerable amount of money. The idea was that for the first three years of reorganization of the journals, rates would not be increased. However, there almost certainly will be an increment in subscription rates next year.

One item in the budget of concern is the audiovisual program. Initially, an investment of $150,000 was authorized by Council. It was anticipated that the income would exceed expenses. However, this level of income has not been realized. Instead, an annual deficit of $30,000 has occurred so that the Society has now invested $98,000 of the authorized $150,000. It was noted that the Society's investment will eventually be recovered because of the value of sales expected after the termination of development expenses.

The above is the same type of loan made 24 years ago for development of the Handbooks. At that time, $250,000 was authorized by Council for the Handbook Series. The expenditures above the cumulative income has been about $200,000, and it

does not appear that costs will exceed $17,000 during 1979. The inventory of the Handbooks is valued at more than the outstanding loan.

As to the increased costs of Society operations for the next year, they are not rising as much as the national average of inflation. The dues increase of $5.00 for Regular, Corresponding, and Associate members, approved last Fall, exempts members who have had their doctoral degrees less than five years.

B. Financial Development Committee

Dr. W.F. Ganong, Chairman of the Financial Development Committee, presented a progress report on the activities of his Committee. The members include Edward L. Alpen, Edward H. Blaine, A. Clifford Barger, Walter F. Garey, and Charles R. Park with the immediate Past President serving as Chairman.

In an effort to decrease dependency on dues, steps have been taken to increase the number of Sustaining Associate members. In addition, foundations are being contacted to support various Society activities.

The system of voluntary contributions from members, initiated last year, has realized $6,700 from 584 members. Emeritus members have been invited to make contributions, and to date, 142 Emeritus members have contributed $1,922. This is a demonstration of the affection members have for the Society. Efforts to obtain voluntary contributions will be continued, and the dues notice will permit members to apply contributions to specific programs.

Individual bequests are being encouraged with regular notices in *The Physiologist* and personal contact among senior physiologists. It is planned to ask all members over 55 to consider the possibility of bequests. For interested individuals, the Society will provide financial and legal advice.

The Endowment Fund, established in 1977, provides a mechanism for funding specific programs, such as the Perkins Fellowship Program, the Bowditch Lecture and the Daggs Award.

C. Publications Committee

Dr. Alfred Fishman, Chairman of the Publications Committee, reported that the Society publications are in excellent shape. He was optimistic that the corner has been turned on reorganization of the *American Journal of Physiology,* and commended his Committee, Drs. Robert Berne and Robert Berliner, and the Publications Manager and his staff.

The number and quality of manuscripts being submitted have improved which indicates satisfaction with the journal. After three years of change, the budget is balanced. The puchase of complete sets of the AJP by libraries provides the financial base for the operation. This allows great flexibility of subdividing into new journals which will probably be a continuing process. Much more important is that the section journals correspond to the Society's sections. The journals are providing new horizons, and the Society and Publications Committee are in a better position to provide for the needs of other groups. The most recent example, recommended by Council, was the division of the *AJP: Endocrinology, Metabolism, and Gastrointestinal Physiology* into two separate journals. Dr. Ernst Knobil has accepted the editorship of *AJP: Endocrinology and Metabolism,* and Dr. L.R. Johnson assumed the editorship of *AJP: Gastrointestinal and Liver Physiology.*

The *Journal of Neurophysiology* has also done well, and in 1980, it will become a monthly journal. The *Journal of Applied Physiology* is solid as a rock.

There is great satisfaction at the moment with the Handbooks which are conforming to schedule and are proceeding with the financial constraints of financing. The Clinical Physiology series is progressing satisfactorily with the first monograph having achieved the return of the investment. The second monograph appears to be financially successful, and the third on pulmonary edema has just been released with early indications that sales of this volume will be extremely successful.

In response to a question related to page charges, Dr. Fishman stated that the Society is very sensitive to page charges which are lower than other journals. If an individual indicates he cannot afford to pay page charges, there is no charge.

D. Membership Advisory Committee

Dr. John Cook, Chairman of the Membership Adivsory Committee, commended the members (Gilbert Castro, Jerry Scott, Irwin Fox, John Fray, and Robert Hyatt) for a thorough and conscientious job. They reviewed 215 applications and 430 supporting letters. Of the 132 applications received for Regular membership, all but seven were recommended, and these seven will be offered Associate membership. There were six outstanding proposals for Corresponding membership. Of the 38 Associate member applicants considered, one student will be offered Student membership, and 39 applications were reviewed for Student membership. Dr. Cook was pleased to announce that these applications will bring the Student membership to 160.

The Membership Advisory Committee has had indepth discussions concerning requirements for Regular membership. The Bylaws state there must be "evidence of having published meritorious and original research in physiology." Notably, the word independent is not included. The reason this has become a problem is apparently in physiology, very few people publish solo papers, and the definition of independence becomes hard to define. The Committee relies very heavily on the originality of the applications and the sponsoring letters. Dr. Cook reiterated that the qualifications for Regular membership is having "published meritorious and original research in physiology." This qualifies a number of individuals who are in their second or third year of postdoctoral work before they have assumed full-time positions. Dr. Cook noted that being a postdoctoral does not disqualify a person from Regular membership. An effort is made to bring young people into the Society, and consequently, there has been an emphasis in lowering the mean age.

Following consideration of the category of Honorary membership, a special committee consisting of Drs. Horace Davenport as Chairman, John Brobeck and Hermann Rahn has been appointed to consider Honorary membership requirements.

E. Committee on Career Opportunities in Physiology

Dr. Bohr announced that Dr. Walter C. Randall has accepted the Chairmanship of the new appointed standing Committee on Career Opportunities in Physiology. One of the objectives will be to obtain information regarding manpower ability and requirements in the profession of physiology. Also, measures will be taken to provide information aimed at maintaining an appropriate balance between the supply and demand of physiologists. Specific charges of the Committee are:

> "This Committee is advisory to Council of the American Physiological Society and serves as a resource for current information regarding availability and needs for appropriately trained physiological manpower. It shall report annually to Council. It should be informed concerning the nature of training processes and the quantity of

trained personnel on an annual basis and should recommend measures to assure proper balance between supply and demand of physiologists. The Committee will consist of seven members, at least half being under the age of 40. The Chairman is to be selected by Council and membership on the Committee will be for a three-year term."

F. Centennial Celebration Committee

The Chairman, Dr. Earl Wood, reported that the tasks and responsibilities of the Centennial Celebration Committee (Horace Davenport, Alfred Fishman, Ralph Kellogg, Gordon Moe, Arthur Otis, Orr E. Reynolds, and M.C. Shelesnyak) is just beginning. The Centennial Year will begin with the 30th International Physiological Congress in 1986 and end with a Centennial Meeting (annual) in 1987. The Publications Committee has been asked to look into the development of a hundred-year history of the Society and American physiology. Histories of Physiology Departments in America and historical vignettes of developments in physiology will be published in *The Physiologist.* To this end, an Editorial Board (Horace Davenport, Arthur Otis and Ralph Kellogg) will write and/or obtain material for publication. The issuance of a commemorative stamp in 1987 honoring Beaumont is being pursued. During the Centennial Year, exhibits and lectures will also be held.

G. Program Committee

The Program Executive Committee (H.M. Goodman, Chairman, Melvin Fregly, and Franklyn Knox) is responsible for the operation of the Program Advisory Committee and the generation of scientific programs of the Society. To provide broad input from the membership, the Program Advisory Committee consists of members representing special interest groups within the Society. This Committee is composed of the following individuals who should be contacted by members wishing to make suggestions for program and symposia topics: Circulation Physiology-Peripheral (Brian Duling), Circulation Physiology-Heart (Eugene Morkin), Comparative Physiology (Bruce Umminger), Environmental Physiology (X.J. Musacchia), G.I. Physiology (M. J. Kushmerick), Neural Control of Circulation (J.W. Manning), Neuroendocrinology (Jospeh Meites), Nervous System (David Carpenter), Physiological Chemistry (Thomas B. Miller, Jr.), Renal Physiology (James A. Schafer), and Respiratory Physiology (N.C. Staub).

To illustrate what a hard-working Committee the Society has, Dr. Fregly reported briefly on a few facts about the present meeting. There were a total of 1,909 abstracts processed. Of these, 1,654 were programmed by APS; 255 were transferred to other societies. Of the 1,654 abstracts programmed by the Society, 1,002 were presented orally and 652 were presented as posters. The Society for Experimental Biology and Medicine contributed 301 abstracts, and the Biomedical Engineering Society contributed 61 abstracts.

So far as the meetings themselves are concerned, APS programed 82 slide sessions, 39 poster sessions, 28 symposia, 1 mini symposium and 5 satellite symposia. To support the symposia, approximately $8,300 was raised by solicitation of outside funds outside the Society.

The Program Committee, at its recent meeting, considered the question of the optimal number of symposia for future Federation Meetings. After some discussion, it was the consensus that 25 to 28 symposia sessions seemed appropriate. The Program Committee would like to know the thoughts of the membership as well as the balance of symposia to ten-minute paper and poster presentations.

The Program Committee welcomes the suggestions of members for future symposia and programs. Each member has a direct input to the Program Committee through the representative of the special-interest groups.

A comment from the audience concerned the printed program not being available until attendees arrived at the meeting, and the Society was urged to mail out future programs in advance. Dr. Reynolds replied that the FASEB Program Committee, chaired by the Federation President-Elect, in response to a request from members that the deadline for submission of abstracts be extended, agreed to move the deadline from early December to early January. This was an experiment. At the request from the floor, a straw vote was taken with a slight majority voting in preference of an early December deadline for receipt of abstracts and receiving the printed program in advance of the meeting.

The matter of conflict in simultaneouus sessions was discussed, and Dr. Reynolds indicated that attempts are being made to use a computer to program abstracts and symposia which would help eliminate this problem. Another isssue of concern to the membership was the extended meeting and lack of interdisciplinary programs at this meeting. It was proposed that the first and last part of the extended meeting be scheduled for those societies wishing to meet alone, and the middle four days for those groups wishing to interact in interdisciplinary sessions. Dr. Reynolds commented that for the next two years, there will be intersociety sessions with five of the six societies meeting together. However, in 1982, it is planned that ASBC and APS will meet in the second cluster of an extended meeting.

H. Public Affairs and Public Information Committee

Dr. Brian Curtis, Chairman of the Public Affairs and Public Information Committee, referred to a handout entitled, "Budget Fever on Capitol Hill" indicating that recent Presidential and Congressional developments suggest hard going this year for all federal budgets including those for biomedical research. Even though the President has spelled out basic research as one of his four major areas of emphasis, it is not known what Congress will do. Dr. Curtis emphasized that it is time for members of the Society to make their presence known to Congress and express their views on the importance of stability in funding. Congressional members are sensitive to their constituency but seldom hear from the scientific community. A sample letter was provided, and Dr. Curtis strongly urged that members use it as a guide in corresponding with their Congressional representatives to make them aware of the needs of science.

VIII. FUTURE MEETINGS

Dr. Bohr reported that future meetings of the Society scheduled to date are:

Spring

April 13-18, 1980 - Anaheim, CA
April 12-17, 1981 - Atlanta, GA
April 18-23, 1982 - New Orleans, LA

Fall

October 15-19, 1979 - New Orleans, LA
October 12-17, 1980 - Toronto, Canada
November 1-6, 1981 - Boston, MA
October 10-15, 1982 - San Diego, CA

Specialty

"Relation Between Neurotransmitters and Endocrine Functions"

August 22-24, 1979 - East Lansing, MI

28th International Congress

July 13-19, 1980 - Budapest, Hungary

A. 1979 Fall Meeting

On behalf of the New Orleans Local Committe, Dr. Nicholas DiLuzio, and himself, Dr. John Spitzer extended a most cordial invitation to the membership to attend the Society Fall Meeting. In addition to the stimulating refresher courses, symposia and paper sessions, it will be found that the social program will be equally exciting. The Local Committee is in the process of planning an evening on the river boat complete with New Orleans jazz. The Departments of Physiology at Louisiana State University Medical Center and Tulane University Medical Center will have open house on Monday, October 15, and all attendees are invited to visit the Medical Centers. Dr. Spitzer promises that the excellent smorgasbord of food for thought will be more than matched by the food for the palate in New Orleans. There will be good weather and an excellent meeting.

B. Society Specialty Meeting

A Society Specilty Meeting, organized by Dr. Joseph Meites and his colleagues, will be held on the Michigan State University campus in the Kellogg Center, August 22-24, 1979. The Endocrine Society and the Society for Neuroscience will be guest societies. The program will include three half-day symposia on "Relation Between Brain Neurotransmission and Endocrine Function," short paper and poster sessions.

C. 1980 International Physiological Congress

Dr. A. Kovach, Secretary-General of the International Union of Physiological Sciences and President of the Hungarian Physiological Society, extended a cordial invitation to all physiologists from the United States to attend the 1980 International Physiological Congress in Budapest, July 13-19. Dr. Kovach announced with pleasure that 1,100 responses to the first announcement of the Congress were received from the United States. The Hungarian Academy of Sciences will provide housing and living expenses for 1,000-2,000 students attending the Congress. The Organizing Committee is working very hard to provide attendees with a high level of scientific and cultural programs.

Dr. W.F. Ganong reported that the U.S. National Committee for the IUPS is composed of five societies (American Physiological Society, Society of General Physiologists, Comparative Physiology Section of the American Society of Zoologists, Society for Neuroscience, and the Biomedical Engineering Society). The U.S. National Committee will initiate a campaign for travel grants in the near future. The deadline for receipt of applications will be November 1, 1979, and applications may be obtained from the U.S. National Committee for IUPS, National Academy of Sciences, Washington, D.C. Announcements of the travel grants program will be carried in the June and August issues of *The Physiologist* and recipients will be notified of their selection in early December. The general contributions of APS members over the last three years will be used solely to support the travel of young scientists in North America. This will, of course, include our Canadian and Mexican Members.

IX. NEW BUSINESS

A. Equal Rights Amendment

A member asked whether the Society Council or Program Committee planned to poll the membership to determine if the Society should meet in cities that had not ratified the ERA Amendment. It was the feeling of this individual that the Council should determine how the membership feels about this issue. Since the ERA situation will be settled within the next five years and APS meeting sites have been selected through 1982, one member seemed to think it was a moot point to poll the membership.

Upon motion made, seconded and carried, it was resolved that the Society membership should be polled concerning the Equal Rights Amendment with respect to the location of future APS meetings.

The Council will receive the results of the poll as a recommendation or expression of opinion concerning the issue.

There being no other business, the 121st Business Meeting of the Society was adjourned at 6:30 p.m., April 8, 1979.

Ernst Knobil, President-Elect

***On advice of legal counsel this action has been deferred to allow council discussion.**

RENAL SECTION NEWS FROM SPRING MEETING

The 1979 Renal Dinner and Business Meeting was held April 8, 1979 at the Fairmont Hotel in Dallas. Our Treasurer for this past year, Gabe Navar, did a superb job of selling tickets and there were no vacant seats. Sid Solomon talked to us about the funding process for science and encouraged us all to be more active in explaining the scientific process and the need to support it to the people in our local communities.

As a particular feature of this year's meeting, the First Annual Awards for Excellence in Renal Research were made to young investigators for work presented at the Fall Meeting of the American Physiological Society in St. Louis. The three winners were graduate students. They were:

Sara Maria Galli-Gallardo, Texas Tech University, Lubbock

Rodney W. Lappe, Indiana University School of Medicine, Indianapolis

Denyse Thornley-Brown, Louisiana State University Med. Ctr., Shreveport

These awards, consisting of a certificate prepared by the American Physiological Society, were presented to the winners by our Chairman for this year, Dick Malvin.

During the business meeting, chaired by Dick Malvin, the only new business acted upon was a resolution to make an effort to offer a reduced price to students for future renal dinners. However, a decision on the method by which this was to be done was left up to the incoming officers. The group then elected officers for the 1979-1980 year. Bill Dantzler, Fred Wright, and Paul Churchill were elected Chairman, Secretary, and Treasurer, respectively. Jim Schafer was elected Program Representative from the Renal Section to the American Physiological Society for a two year period. The meeting was then adjourned.

The officers are interested in any ideas you have about the activities of the Renal Section or the annual dinner. Please feel free to contact any one of us about any appropriate matter.

William H. Dantzler
Secretary, Renal Section, 1978-79
Chairman, Renal Section, 1979-80

MEMBERSHIP STATUS

Regular Members	4,160
Retired	452
Honorary	9
Associate	638
Corresponding	34
Student	121
	5,414

DEATHS REPORTED SINCE THE 1978 FALL MEETING

William G. Clark (R) - 2-13-79 - VA Hosp., Sepulveda, CA
Hiram E. Essex (R) - 12-15-78 - Mayo Clinic, Rochester, MN
Otto H. Gauer - 1-22-79 - Berlin, Germany
David E. Haft - 2-11-79 - New York Med. Coll.
Harold Higgins (R) - - Newton Centre, MA
Joe W. Howland (R) - 10-12-78 - Chapel Hill, NC
F.R. Hunter - 9-29-78 - Univ. of Pacific, Stockton, CA
Dwight J. Ingle (R) - 7-28-78 - Rapid City, MI
W.R. Ingram (R) - 12-26-78 - Univ. Of Iowa, Iowa City
Daniel V. Kimberg - 11-26-78 - Columbia Univ., New York City
William B. Kinter - 10-5-78 - Salsbury Cove, ME
Milton O. Lee (R) - 11-19-78 - Sarasota, FL
Karl Lowy - 9-9-78 - Univ. of Rochester, Rochester, NY
Francis Lukens (R) - 12-4-78 - Pittsburgh, PA
Kehl Markley III - 2-28-79 - NIH, Bethesda, MD
A.R. McIntyre (R) - 9--79 - Univ. of Nebraska, Omaha
John Remigton (R) - 10-30-78 - Atlanta, GA
Jacob Sacks - 10 -- 78 - Fayetteville, AR
William Scarborough (R) - 1-10-79 - Rockville, MD
James Schwinghamer - 12-21-78 Michigan State Univ., East Lansing
John C. Scott (R) - 9-9-78 - Hahnemann Med. Coll., Philadelphia
Robert Emrie Smith (R) - 1-1-79 - Univ. of California, Davis
Irving H. Wagman - -- Univ. of California, Davis
(R) - Retired

FIFTY-YEAR MEMBERS AND YEAR OF ELECTION

Adolph, Edward F., 1921 (E)
Baetjer, Anna M., 1929 (E)
Bergeim, Olaf, 1916 (E)
Bing, Richard J., 1922 (R)
Bourquin, Helen, 1925 (R)
Boyd, T.E., 1925 (E)
Brooks, Matilda, 1927 (R)
Cattell, McKeen, 1923 (E)
Chen, K.K, 1929 (R)
Davis, Hallowell, 1925 (R)
Dragstedt, Carl A., 1928 (E)
Friedman, Maurice H., 1929 (R)
Gemmill, Chalmers L., 1928 (E)
Gilson, Arthur S., 1927 (E)
Greisheimer, Esther M., 1925 (E)
Grollman, Arthur, 1925 (E)
McCouch, Grayson P., 1925 (E)
Minot, Ann S., 1923 (E)
Necheles, Heinrich, 1929 (E)
Pond, Samuel E., 1924 (E)
Redfield, Alfred C., 1919 (E)
Reznikoff, Paul, 1927 (E)
Richter, Curt P., 1924 (E)
Ryan, Andrew H., 1912 (E)
Schmidt, Carl F., 1929 (E)
Gross, Erwin G., 1927 (E)
Hastings, Albert B., 1927 (E)
Hayman, Joseph M., Jr., 1928 (E)
Hertzman, Alrick B., 1925 (E)
Hinrichs, Marie A., 1928 (R)
Hinsey, Joseph C., 1929 (E)
Hitchcock, Fred A., 1927 (R)
Irving, Laurence, 1927 (R)
Jackson, Dennis E., 1910 (E)
Jacobson, Edmund, 1929 (R)
Johnson, Jane Sands Robb, 1925(E)
Kleitman, Nathaniel, 1923 (E)
Koppanyi, Theodore, 1924 (E)
Landis, Eugene M., 1928 (E)
Magath, Thomas B., 1928 (E)
Mayerson, H.S., 1928 (R)
Smith, Erma A., 1928 (E)
Starr, Isaac, 1929 (R)
Still, Eugene U., 1928 (E)
Tainter, Maurice L., 1929 (E)
Van Liere, Edward J., 1927 (E)
Visscher, Maurice B., 1927 (E)
Wearn, Joseph T., 1921 (E)
Wyman, Leland C., 1927 (E)
(E) - Emeritus
(R) - Regular

NEWLY ELECTED MEMBERS

The following, nominated by Council, were elected to membership in the Society at the Spring Meeting, 1979.

REGULAR MEMBERS

ADDONIZIO, V. Paul: Res. Felllow, Dept. Surg., Univ. of Pennsylvania, Philadelphia

ANDRESEN, Michael C.: Dept. Physiol. & Biophys., Univ. of Texas Med. Br., Galveston

ARONSON, Peter S.: Dept. Med., Yale Sch. Med., New Haven, CT

BARANY, Kate: Assoc. Prof., Dept. Physiol. & Biophys., Univ. Illinois, Chicago

BARBER, Billy J.: Dept. Physiol., Univ. of Mississippi Med. Ctr., Jackson

BARFUSS, Delon W.: 5129 Goldmar Dr., Birmingham, AL

BARRY, William H.: CV Div., Peter Bent Brigham Hosp., Boston

BESCH, Henry R., Jr.: Indiana University Sch. Med., Indianapolis, IN

BHATTACHARYYA, A.K.: Dept. Pathol. & Physiol., Louisiana State Univ., New Orleans

BOWEN, John C.: Ochsner Clinic, New Orleans

BUERKERT, John E.: Dept. Med., Washington Univ. Sch. Med., St. Louis

BURSE, Richard L.: Altitude Res. Div., US Army Res. Inst. Environ. Med., Natick, MA

CARLSON, Drew E.: Dept. Biomed. Engr., Johns Hopkins Univ., Baltimore

CHERRINGTON, Alan D.: Med. Ctr., Vanderbilt Univ., Nashville, TN

CHESNEY, Russell W.: Dept. Pediat., Univ. Wisconsin Ctr. Hlth Sci., Madison

CHIARANDINI, Dante J.: Dept. Ophthal. & Physiol., New York Univ. Med. Ctr., NYC

COHEN, Allen B.: Temple Univ. Hosp. Philadelphia

COLEMAN, Marilyn A.: Dept. Poultry Sci., Ohio State Univ., Columbus

COOKE, Helen J.: Dept. Physiol., Univ. of Kansas Med. Ctr., Kansas City

CRAPO, James D.: Dept. Med., Duke Univ. Med. Ctr., Durham, NC

CRUZ, Julio C.: Res. Assoc., CV Pulm. Res. Lab., Univ. of Colo. Med. Ctr., Denver

DANIELE, Ronald P.: Dept. Med. & Pathol, Univ. of Pennsylvania, Philadelphia

DEY, Sudhansu K.: Dept. GYN/OBST, Kansas Univ. Med. Ctr., Kansas City

DINOSO, Vincente P., Jr.: Dept. Med., Hahnemann Med. Coll., Philadelphia

DREES, John A.: Dept. Physiol. & Biophys., Temple Univ. Hlth. Sci. Ctr., Philadelphia

ENGELAND, William: Res. Fellow, Johns Hopkins Univ. Sch. Med., Baltimore

EPSTEIN, Mary Anne: Dept. Chem. Engr., Columbia Univ., NYC

EPSTEIN, Ralph A.: Assoc. Prof., Columbia Univ., NYC

FALVO, Richard E.: Assoc. Prof., Southern Illinois Univ., Carbondale

FERGUSON, James L.: Dept. Physiol. & Biophys., Univ. of Illinois, Chicago
FULLER, Charles A.: Div. Biomed. Sci., Univ. of California, Riverside
GALLIN, Elaine: Res. Physiologist, Armed Forces Biol. Res. Inst., Bethesda, MD
GALLO-TORRES, Hugo, Dept. Biochem. Nutr., Roche Res. Ctr., Nutley, NJ
GALVIN, Michael J. Jr., Leb. Br., NIEHS, Res. Triangle Pk., NC
GARDNER, Jerry D.: Digestive Dis. Br., NIH, Bethesda, MD
GEE, Marlys H.: Dept. Physiol., Jefferson Med. Coll., Philadelphia
GLANTZ, Stanton A. Dept. Med., Univ. of California, San Francisco
GODT, Robert E.: Dept. Physiol., Med. Coll. Georgia, Augusta
GOUGH, William B.: Dept. Med. & Physiol., Hahnemann Med. Coll., Philadelphia
GRANDISON, Lindsey J.: Dept. Physiol., Rutgers Med. Sch., Piscataway, NJ
GRAY, Barry A.: Dept. Med., Univ. of Oklahoma Hlth. Sci. Ctr., Oklahoma City
GUMUCIO, Jorge J.: Dept. Int. Med., Univ. of Michigan, Ann Arbor
HALDAR, Jaya: Dept. Pharmacol., Columbia Univ., Coll. P & S, NYC
HARMON, John W.: Div. Surg., Walter Reed Army Med. Ctr., Washington, DC
HAYS, Elizabeth T.: Dept. Biol., Nazareth Coll. of Rochester, NY
HECHTMAN, Herbert B.: Dept. Surg., Peter Bent Brigham Hosp., Boston
HELLER, Lois J.: Dept. Physiol., Univ. of Minnesota Sch. Med., Duluth
HESS, David L.: Asst. Scientist, Oregon Reg. Primate Res. Ctr., Beaverton
HOPKINS, Carl D.: Dept. Ecol. & Behav. Biol., Univ. of Minnesota, Minneapolis
JOHNSON, Alan K.: Dept. Psychol., Univ. of Iowa, Iowa City
JOSE, Pedro A.: Assoc. Prof., Georgetown Univ. Sch. Med., Washington, DC
KAHN, Thomas: Dept. Med., Mount Sinai Sch. Med., CUNY, NYC
KAPLAN, Jack H.: Dept. Physiol. & Biophys., Univ. of Iowa, Iowa City
KEELY, Stanley, Jr.: Dept. Physiol., Vanderbilt Univ. Sch. Med., Nashville
KHAN, Mushtag A.: Div. Toxicol., FDA, Washington, DC
KING, Malcolm: Christie Labs., McGill Univ., Montreal
KOLBECK, Ralph C.: Dept. Med., Med. Coll. of Georgia, Augusta
KUMARESAN, Perianna: Horm. Labs., SUNY, Downstate Med. Ctr., Brooklyn
LAI-FOOK, Stephen J.: Dept. Physiol. & Biophys., Mayo Clinic, Rochester, MN
LEFLORE, William B.: Dept. Biol., Spelman Coll., Atlanta, GA
LO, Chu-Shek: Asst. Prof., Uniformed Services Univ., Bethesda, MD
LOEPPKY, Jack A.: Assoc. Scientist, Lovelace Med. Fndn., Albuquerque, NM
LOEWY, Arthur D.: Dept. Anat., Washington, Univ., St. Louis
LUFT, Friedrich C.: Dept. Med., Indiana Univ. Sch. Med., Indianapolis
LYNCH, James C.: Dept. Physiol., Mayo Med. Sch., Rochester, MN
MANN, David R.: Dept. Physiol., Morehouse Coll. Med., Atlanta, GA
MANNING, Roy D., Jr.: Dept. Physiol. & Biophys., Univ. of Mississippi, Jackson
MARTIN, Henry F. III: Dept. Physiol., Med. University of SC., Charleston
McDANIEL, Huey G.: Diabetes Res. Lab., VA Hosp., Birmingham, AL
MEYERS, Kenneth M.: Dept. Physiol., Washington State Univ., Pullman
MICHAEL, Lloyd H.: Dept. Med., Baylor Coll. Med., Houston, TX
MICHELSON, Eric L.: Res. Fellow Cardiol., Hosp. of Univ. of Pennsylvania
MILLEN, John E.: Dept. Med., Med. Coll. of Virginia, Richmond
MORGANROTH, Joel: Dept. Cardiol., Lankenau Hosp., Philadelphia
MORTOLA, Jacopo P.: Dept. Physiol., McGill Univ., Montreal
MULDOON, Sheila M.: Dept. Anesthesiol. & Physiol., Uniformed Services Univ. of Hlth Sci., Bethesda, MD
MURTHY, K.S. Krishna: Dept. Neurosurg., Univ. of Texas Med. Sch., Houston
MYHRE, Loren G.: Res. Physiologist, USAF Sch. Aerospace Med., Brooks AFB, TX
NORMAN, Roger A., Jr.: Dept. Physiol., Univ. of Mississippi, Jackson
OPAVA-STITZER, Susan: Dept. Physiol., Univ. of Puerto Rico, San Juan
OREM, John M.: Dept. Physiol., Texas Tech Univ., Lubbock
ORMSBEE, Herbert III: Dept. Surg. & Physiol., Univ. of Maryland, Baltimore
PARKHIE, Mukund R.: 790 Westside Dr., Gaithersburg, MD
PEISSNER, Lorraine C.: Dept. Physiol., Kirksville Coll. Osteo. Med., Kirksville, MO
PENNOCK, Bernard E.: Dept. Med., Univ. Oklahoma Sci. Ctr. Oklahoma City, OK
PITKOW, Howard S.: Dept. Physiol. Sci., Pennsylvania Coll. Podiat. Med., Philadelphia
RANDALL, David J.: Dept. Zool., Univ. of British Columbia, Vancouver
ROSS, Charles D.: Dept. Physiol., Oral Roberts Univ. Sch. Med., Tulsa
SATO, Kenzo: Dept. Dermatol., Univ. of Iowa Hosps., Iowa City
SCHWARTZ, Jessica: Dept. Physiol., Emory Univ. Sch. Med., Atlanta
SCHWARTZKROIN, P.A.: Dept. Neurol. Surg., Univ. of Washington, Seattle
SLOANE, Bonnie F.: Dept. Physiol., Univ. of Pennsylvania, Philadelphia
SMITH, Edgar N.: Dept. Biol., Northeastern Univ., Tahlequah, OK
SPANGLER, Stanley G.: Dept. Physiol. & Biophys., Univ. of Alabama, Birmingham
SPIELMAN, William S.: Dept. Physiol., Mayo Med. Sch., Rochester, MN
STEPHENS, Gergory A.: Dept. Physiol., Univ. of Delaware, Newark
STERN, Judith: Dept. Nutr., Univ. of California, Davis
STOWE, Nicholas T.: Dept. Hypertension & Nephrol., Cleveland Clinic Fndn.

STUESSE, Neurobiol. Prog., N.E. Ohio Univ., Rootstown
SUTTON, John R.: Dept. Med., McMaster Univ., Hamilton, Ont., Canada
SYLVESTER, Jimmie T.: Dept. Med., Johns Hopkins Hosp., Baltimore
TAI, Yuan-Heng: Res. Physiologist, Walter Reed Army Inst. Res., Washington, DC
TANNENBAUM, Gloria: Dept. Med., MGill Univ., Montreal
TAUBERT, Kathryn A.: Dept. Physiol., Univ. of California, Riverside
TERRANOVA, Paul F.: Dept. Physiol., Univ. Kansas Med. Ctr., Kansas City
THIES, William H.: Dept. Physiol., Indiana Univ. Sch. Med., Terre Haute
THORNER, Michael O.: Assoc. Prof., Univ. of Virginia, Charlottesville
THORNHILL, James A.: Fac. Med., Univ. of Calgary, Calgary, Alb., Canada
TORRE-BUENO, Jose: Dept. Physiol., Duke Univ. Med. Ctr., Durham, NC
TUMA, Ronald F.: Dept. Physiol., Temple Univ. Sch. Med., Philadelphia
TURNER, Terry T.: Dept. Urology, Univ. of Virginia, Charlottesville
VARON, Myron I.: A.L.S. Soc. America, Sherman Oaks, CA
VAUGHAN, Mary K.: Dept. Anat., Univ. Texas Hlth. Sci. Ctr., San Antonio
VAUGHN, Linda K.: Postdoct. Fellow, Univ. of Calgary, Alb., Canada
WALLING, Marlin W.: VA Wadsworth Hosp. Ctr., Los Angeles, CA
WARD, Walter F.: Dept. Physiol., Univ. Texas Hlth. Sci. Ctr., San Antonio
WARNOCK, David: Dept. Med., Univ. of California Med. Ctr., San Francisco
WEI, Enoch P.: Dept. Med., Med. Coll. Virginia, Richmond
WEINBERG, Sheila R.: Res. Invest., Armed Forces Radiobiol. Res. Inst., Bethesda, MD
WHITE, John F.: Dept. Physiol. Emory Univ. Atlanta, GA
WIDDICOMBE, Jonathan: CV Res. Inst., Univ. of California, San Francisco
WILLIAMS, Darrell D.: Vis. Scientist, Univ. of Washington, Seattle
WRAY, Harvey L.: Dept. Med., Walter Reed Army Med. Ctr., Washington, DC
WU, Ai-Lien: NIAMDD, NIH, Bethesda, MD
ZARET, Barry L.: Dept. Med., Yale Univ. Sch. Med; New Haven, CT.

CORRESPONDING MEMBERS

ANGIELSKI, Stefan: Dept. Clin. Biochem., Md. Acad., Gdansk, Poland
COLINA-CHOURIO, Jose: Dept Physiol., Univ. del Zucia, Maracaibo, Venezuela
HUDLICKA, Olga: Dept. Physiol., Univ. of Birmingham, Birmingham, England
MANOHAR, Murli: Dept. Cardiopul. Physiol., Univ. Illinois Vet. Med., Urbana
ROSENDORFF, Clive: Dept. Physiol., Univ. Witwatersrand, Johannesburg, South Africa
THURAU, Klaus W.C.: Dept. Physiol., Univ. of Munich, Pettenkoferstr., Munchen

ASSOCIATE MEMBERS

AULICK, Louis H.: Inst. Surg. Res., Brooke Army Med. Ctr., Fort Sam Houston
BARNES, Karen L.: Res. Div., Cleveland Clinic Fndn.
BENNETT, Frederick: Dept. of Physiol., Dartmouth Med. Sch. Hanover, NH
BEYER-MEARS, Annette: New Jersey Med. Sch., Newark
BOYD, Thomas A.: Hershey Med. Ctr., Pennsylvania State Univ., Hershey
BRITTON, Steven L.: Mayo Clinic, Rochester, MN
CASSIDY, Sharon S.: Dept. Med. & Physiol., Univ. of Texas Hlth. Sci. Ctr., Dallas
CONNORS, John M.: Res. Assoc., West Virginia Univ., Morgantown
ESTES, James E.: Res. Fellow, Albany Med. Coll., Albany, NY 12208
FLORANT, Gregory L.: Dept. Neurol., Swarthmore Coll., Swarthmore, PA
GATTO, Louis A.: Dept. Biol., State Univ. of N.Y., Cortland
GULLNER, Hans-Georg: VA Hosp., Res. Service, San Antonio, TX
JEVNING, R.: Dept. Med., Univ. of California, Irvine
KALLOCK, Michael J.: Res. Fellow, Mayo Clinic, Rochester, MN
KRAUSE, Brian R.: Dept. of Physiol., Louisiana State Univ.,
LAUDENSLAGER, Mark: Res. Psychol., Univ. California, Santa Barbara
LECHNER, Andrew J.: Dept. Physiol., Univ. Colorado, Denver
LIGHT, Kim E.: Dept. Physiol., Texas Tech Univ. Sch. Med., Lubbock
LINDSTEDT, Stan L.: Dept. Physiol., Univ. of Arizona, Tucson
MARAN, Janice W.: Dept. Pharmacol., McNeil Labs., Ft. Washington, PA
MARSHALL, Leslie B.: Dept. Physiol. & Biophys., Univ. of Iowa, Iowa, City
MARTIN, John S.: Dept. Physiol. & Biophys., Temple Univ., Philadelphia
PETERSON, Barry T.: Div. Pul. Med., Vanderbilt Univ., Nashville, TN
POHL, Clifford R.: Dept. Physiol., Univ. of Pittsburgh Sch. Med.
POWELL, Frank L. Jr.: Dept. Med., Univ. of California, San Diego
RANKIN, James S.: Dept. Surg., Duke Univ. Med. Ctr., Durham, NC
REYNOLDS, David B.: Mayo Clinic & Fndn., Rochester, MN
ROBERTS, Mary M.H.: Miami Valley Labs., Cincinnati, OH
SELF, Luther E. Louisiana State Univ., Shreveport
SHLEVIN, Harold H.: Dept. Pharmacol., Mayo Fndn., Rochester. MN
SMITH, Thomas J.: Dept. Surg., Clin. Sci. Ctr., Univ. of Wisconsin, Madison
STAATS, Bruce A.: Thoracic Dis., Mayo Clinic, Rochester, MN
STAMFORD, Bryant A.: Exercise Physiol. Lab., Univ. of Louisville, KY
STEGE, Thomas E.: Dept. Zool., Ohio Wesleyan Univ. Delaware, OH
STRAHLENDORF, Jean: Dept. Physiol., Texas Tech Univ., Lubbock
TABORSKY, Gerald, Jr.: Div. Endo. & Metab., VA Hosp., Seattle
WHALL, Clifford, Jr.: Dept. Physiol., Univ. of Michigan, Ann Arbor
WHITE, Timothy P.: Dept. Phys. Ed., Univ. of Michigan, Ann Arbor

ZUCKER, Albert H.: Dept. Physiol. & Biophys., Univ. Tennessee Ctr. Hlth. Sci., Memphis

STUDENT MEMBERS

ADAIR, Thomas H.: Univ. of Texas Med. Br., Galveston
ADAMS, Richard P.: University of Tennessee, Knoxville
ASHTON, Juliet, H.: Univ. of Texas Hlth. Sci. Ctr., Dallas
BARBER, Michael J.: Res. Asst., Loyola Univ. of Chicago, Maywood, IL
BELL, Phillip D.: Dept. of Physiol., Univ. of Alabama, Birmingham
BUTLER, Bruce D.: Dept. Physiol., Univ. of Texas Med. Br., Galveston
COPMANN, Thomas L.: Dept. Biol. Sci., Kent State Univ., Kent, OH
COTE, Richard III: Human Perf. Lab., USAF Acad., CA
CUNNINGHAM, Susanna: Dept. Physiol. Nursing, Univ. of Washington, Seattle
EBERT, Thomas J.: Dept. of Physiol., Med. Coll. Wisconsin, Wauwatosa
ECHTENKAMP, Stephen: Dept. Physiol. & Biophys., Univ. Nebraska, Omaha
FISCHETTE, Christine: Physiol. Dept., Coll. Med. & Dent. of N.J., Newark
FISHER, John T.: Dept. Physiol., McGill Univ., Montreal
FUNCH, Paul G.: Dept. Physiol., State Univ. of NY at Buffalo
GARBER, David W.: Hershey Med. Ctr., Pennsylvania State Univ., Hershey
GLENN, Loyd: Dept. Psychiat., Stanford Univ., Stanford, CA
GULEFF, Patrica S.: Res. Assoc., Worcester Fndn. Exptl. Biol., Shrewsbury, MA
HANCK, Dorothy A.: Dept. Physiol., Temple Hlth. Sci. Ctr., Philadelphia
HARTUPEE, Dale A.: Res. Fellow, Mayo Clinic & Fndn., Rochester, MN
HOUCK, Peter C.: Dept. Physiol., Texas Tech Univ., Lubbock
JENSEN, Ralph C.: Dept. Physiol., Johns Hopkins Univ., Baltimore
KOCH, John C.: University of Michigan, Ann Arbor
LYDIC, Ralph B.: Dept. Physiol., Texas Tech Univ., Lubbock
MAHANY, Thomas M.: Georgetown Univ., Dept. Physiol. & Biophys., Washington, DC
McCALEB, Michael L.: Dept. Pharmacol., Univ. North Carolina, Chapel Hill
McCOY, Frank P.: Dept. Physiol., Louisiana State Univ. Med. Ctr., New Orleans
MELLOW, Alan M.: Dept. Pharmacol., Northwestern Univ. Med. Sch., Chicago
MRAS, Suzanne: Dept. Physiol., Univ. of South Florida, Tampa
NELSON, Mark T.: Dept. Physiol. & Biophys., Washington Univ., St. Louis
PAULSON, Dennis J.: Dept. Physiol., Texas Tech Sch. Med., Lubbock
POMERANTZ, Kenneth B.: Dept. Physiol. & Biophs., Georgetown Univ., Washington, DC
RAY, Richard H.: Dept. Physiol., Med. Coll. of Georgia, Augusta
SHORS, Edwin C.: Univ. of Southern California, Los Angeles
SIT, Siu Po: Dept. of Physiol., Michigan State Univ., East Lansing
STRAHLENDORF, Howard K.: Dept. Physiol., Texas Tech Univ., Lubbock
STUDER, Rebecca K.: Univ. of Pittsburgh Sch. Med., Pittsburgh, PA
WEINBERG, Richard J.: Dept. of Physiol., Univ. of Washington, Seattle
WESLEY, Charles R.: Dept. Physiol., USC Sch., Columbia, SC
WILLIAMS, Wesley M.: Ctr. Brain Res., Univ. of Rochester, NY

APS SUSTAINING ASSOCIATES

In these days of inflation and multiplication of the factors forcing increased dues, the American Physiological Society owes a special debt of gratitude to its Sustaining Associates. The Sustaining Associate category of membership was established in 1960 by a Bylaw which states that "individuals and organizations who have an interest in the advancement of biological investigation may be invited by the President, with the approval of Council, to become Sustaining Associates."

In the past, much of the financial support contributed by the Sustaining Associates has been used by the Society for support of its education program. Activities requiring special support have included visiting lectureships, teacher workshops, career information brochure development and distribution, education materials development, and special educational programs at the Spring and Fall Society meetings. From time to time, certain of these programs have attracted grant and contract support, but continued support by Sustaining Associates has enabled the Society to maintain continuity in its educational program.

Donations from Sustaining Associates also support the general activities of the Society, and the scientific program at the Spring and Fall meeting. Since the Society works in many different ways to foster physiology and scientific research in general, the dollars contributed pay important dividends in terms of benefits to science and the entire scientific community.

Our Society is indebted to the following past and present Sustaining Associates:

Abbott Laoratories
Ayerst Laboratories
Beckman Instruments, Inc.
Burroughs Wellcome Company
CIBA-GEIGY Corporation
Ethicon Inc.
Gilford Instrument Laboratories, Inc.
Gilson Medical Electronics
Grass Instrument Company
Hoechst-Roussel Pharmaceuticals Inc.
Hoffmann-La Roche Inc.
Lakeside Laboratories, Inc.
Eli Lilly and Company
Merck Sharp and Dohme
Narco Bio-Systems, Inc.
Norwich Pharmacal Company
Pifzer, Inc.
Phipps and Bird, Inc.
Precision Scientific Company
Riker Laboratories, Inc.
A.H. Robin Company, Inc.
Sherman Laboratories
Smith Kline and French Laboratoratories
Squibb Institute
Tektronic Inc.
Upjohn Company
Warner-Lambert/Park-Davis
Waverly Press, Inc.
Wyeth Laboratories, Inc.

RAY G. DAGGS AWARD

It is with great pride and immense satisfaction that the American Physiological Society proffers to John Richard Pappenheimer the Daggs Award for distinguished service to our Society and signal contributions to our discipline.

John Pappenheimer, educated at Harvard and Cambridge, began his formal career in Physiology at the College of Physicians and Surgeons, an activity interrupted during the war years by service at the Johnson Foundation, in Philadelphia. After the war he returned to Harvard as an Associate in Physiology and now is the George Higginson Professor of Physiology at the Harvard Medical School, the Chair previously occupied by Walter Cannon and Eugene M. Landis. John Pappenheimer's many contributions to cardiovascular, renal and pulmonary physiology have been recognized by election to the National Academy of Sciences and the American Academy of Arts and Sciences and will not be recounted here.

He was the first Bowditch lecturer of the Society, became an influential member of Council and was elected to the Presidency of the American Physiological Society in 1964. He played a major role in launching the immensely successful Handbook of Physiology and served as Chairman of the Handbook Committee from 1972 to 1978. In addition, he labored on the editorial boards of the American Journal of Physiology and of Physiological Reviews as well as serving a term as Associate Editor of Circulation Research.

He was a program director of the 24th International Congress of Physiological Sciences and contributed to Physiology in many other public and private capacities including service on the Council of the International Union of Physiological Sciences, on the Board of Scientific counselors of the National Heart Institute and the Board of Governors of the American Institute of Biological Sciences. Professor Pappenheimer embodies the best in American Physiology. Characteristically, he continues to explore new frontiers, to respond to new scientific challenges and remains astride the ever expanding boundaries of our discipline.

Dr. Pappenheimer:

"In the course of a long career, one is likely to belong to a number of societies, but I have always regarded the American Physiological Society as the primary society to which I am most indebted. The first meeting of APS I attended was in New Orleans in 1940 after having spent three years in England. I presented a ten-minute paper on something about the diversion of blood from metabolizing tissue and muscle when you stimulate the vasoconstrictor nerves. I did not know anyone at the meeting, but Dr. Harry Bazzet very kindly invited me to dinner with the Circulation Group. I went at the appointed hour and made polite conversation with various strangers. Time passed, but Dr. Bazzet never arrived. After making inquiries, I learned I was at the meeting of the American Association of Cotton Growers.

At that same meeting, Pete Scholander, recently from Norway, presented a paper on the diversion of blood away from metabolizing muscles of the seal when you made it dive. I was fascinated by this because I thought it related to my own less spectacular work. I introduced myself, and we compared notes. In the end, Dr. Scholander invited me to go with him to Florida to study the manatee. When we left the following week, it was the beginning of a long and delightful association. I owe the American Physiological Society many such wonderful friendships over the years.

Somewhate later came my service on Council. I recall great pleasure in relationships with my fellow Councilors - Hy Mayerson, Hermann Rahn, Robert Forster, and Jack Brookhart.

The most satisfying program with which I have been involved is the Perkins Fellowship. When Johnny Perkins died in 1966, his wife wanted a memorial to him and established the Perkins Fellowships, administered by the APS. This program is unique in that it supports the wives and families of visiting scientists and makes it possible for them to have a pleasant stay while in the U.S. So far, these fellowships have gone to the families of 24 visiting scientists, including 65 children, from 14 different countries. I feel this has done a great deal of good, far transcending physiology itself, because the children go home and remember it all their lives and tell their friends how the fellowships helped them.

Soon we will have our 100th birthday, and I hope it can be made a nice family party. Many of our daughters have left us and have married people with such names as Neuroscience, Biophysics, Biomedical Engineering, and other such names. When 1987 arrives, I hope our daughters will join us and provide the best of physiology and that we can enjoy the meeting with a sense of fun as well as history."

Recipients of the Daggs Award
1974 - John H. Brookhart
1975 - Maurice B. Visscher
1976 - James D. Hardy
1977 - Julius H. Comroe
1978 - Hermann Rahn

HONORS AND AWARDS

Fifteen foreign scientists were honored by the National Academy of Sciences by election to membership. APS member **Cornelis A.G. Wiersma** (Netherlands), Professor of Biology, California Institute of Technology, Pasadena, was a recipient of this honor.

Three APS members were elected to membership in the National Academy of Engineering. **Yuan-Cheng B. Fung,** University of California, San Diego for contributions to the theory of elasticity and aeroelasticity, and applications to bioengineering. **A. Pharo Gagge,** Yale University, contributions to the basic principles of air conditioning and bioengineering of heat transfer in man. **Otto H. Schmitt,** University of Minnesota, Minneapolis, pioneering contributions in the development of bioengineering and biophysics and in the interdisciplinary science including vectorcardiography, bioelectricity, and electronic circuitry.

NOTES FROM CAPITOL HILL

Brian A. Curtis, Chairman
Committee on Public Affairs and Public Information

With the regularity of the seasons, Spring brings cherry blossoms and budget debates to Washington. This Spring has been cool, the blossoms have lasted longer; the debate has been very hot and shows signs of lasting all summer.

In mid May the process is well underway. The President's budget message called for strong emphasis on basic research. His budget shows level funding for NIH!

In the Congressional Budget process, biomedical research falls into the category of controllable health expenditures. This function won a 268 million dollar increase over the President's budget. Biomedical research will have to compete with many other activities, including Medical School capitation, for these increased funds.

The Appropriations Subcommittees have completed their hearings. Ernie Knobil, APS President, testified on behalf of Child Health and Human Development in the FY79 supplement and I testified on the FY80 budget. Here are some excerpts from my testimony before the House Subcommittee:

"Biomedical Research Policy has been set by this Subcommitte for many years; numerous advances in science and medicine rest on foundations built in this room. Proof of this leadership can be found in the Aministration's FY80 Budget. In spite of a high priority given basic research in general, biomedical research is singled out for level funding. Why? I believe it is the President's acknowledgment of the leadership of this Subcommittee.

"*Investigator Initiated Research Grants* are the very heart of the nation's biomedical research effort. Research grant funding, particularly new commitments, has experienced large fluctuations in recent years, yet little real growth. The number of new and competing renewal grants funded has remained fairly steady in the last two years at about 5,000. The Administration's budget calls for this number to drop to about 2,300 in FY80. Such a large fall would have disastrous effects and would result in only about 20-23% of the *approved* reseach grants funded.

"It is not difficult to predict the impact of this trend on the national biomedical research enterprise or on the morale of the people whose lives are bound up in it, or on the outlook of those young people who are thinking of joining it. Or, for that matter, on all of us who see in the research enterprise the only hope for an answer to disease. Such a low funding rate might well be taken as a signal of Congressional intent to dismantle the current, highly successful biomedical research enterprise.

"Therefore, we strongly recommend a budget for each institute which will help maintain the numbers of competing grants at least at the current level. We realize this is not a year for much real growth. These modest increases, to maintain previous programs at a constant level, will give us what we need most to contribute to the nation's future health, stability.

"Research Training is a small, but very important, component of the biomedical research effort. Congress voted to allow NSRA Fellowship stipends to rise above the poverty level. Twenty-seven million dollars will be needed for this vital task.

The Biological Reserch Support Grants (BRSG) are important mortar to hold the larger framework of biomedical science together. FASEB applauds this Subcommittee's support of this vital program through the lean years when it did not appear in the budget. Your faith in the program has been, in our view, richly justified. A modest increase in this program would be handsomely repaid."

The House Appropriations Subcommittee markup gives NIH 305 million dollars over the President's budget, a hopeful sign. The Senate markup is scheduled for early June.

The season on budget cutting amendments is now over, only to be replaced by a season of appropriation cutting. Continued effort will be necessary - continued contact with your Congressional delegation is of great importance.

ANNUAL REVIEW OF PHYSIOLOGY

For the past four decades the *Annual Review of Physiology* has been dedicated to the ideal of the intellectual unity of this branch of biology. Early on, a brief sequence of volumes (e.g. 3 through 5) could reasonably attempt to provide critical reviews of every frontier in physiology. The range and diversity of contemporary physiology, however, demand an intense specialization of virtually all its practitioners. Once an integral science, physiology has been transformed into a complex of interrelated sciences with evolving boundaries. The establishment of the *Annual Review of Neuroscience* attests to the need for expanded coverage of what was once a subdivision of physiology.

In the judgment of the Editorial Committee, the time has come to inaugurate a new format recognizing the major subsectors that now exist in physiology. Beginning with Volume 41 (1979), the *Annual Review of Physiology* was divided into sections as follows: Circulation (edited by Robert Berne), Respiration (ed. Alfred Fishman), Endocrinology and Metabolism (ed. Samuel McCann), Renal and Electrolyte (ed. Thomas Andreoli), Cell and Membrane Physiology (ed. John Gergely), Comparative and Integrative Physiology (ed. William Dawson), and Gastrointestinal and Nutritional Physiology (ed. Stanley Schultz), in addition, each volume will contain a Special Topics Section, the first deals with Neurophysiology (ed. Arthur Karlin).

The Editorial Committee will function as a group as before, but now each section editor will formulate themes to be covered by a series of complementary articles emphasizing his sector's most timely and important developments. Thus the traditional single volume will maintain unity while encouraging, by the juxtaposition of sudomains, a crosspollination of interests. The new format must benefit both the active researcher and the specialized scholar; for the generalist - the bravest of scholars - it will be possible to delve into all of the major branches represented in each issue.

We are confident that in its forward-looking new guise the *Annual Review of Physiology* will continue to reach the high levels of quality and utility achieved annually by its predecessor volumes since 1939, and that it will provide the accustomed excellent service to its diverse and ever-expanding audiences in the physiological science for years to come.

AMERICAN PHYSIOLOGICAL SOCIETY
30th ANNUAL FALL MEETING
OCTOBER 15-19, 1979

The 30th Annual Fall Meeting of the American Physiological Society with the Commission on Gravitational Physiology-IUPS and the Biosciences Section of the Gerontological Society as guest organizations, will be held at the New Orleans Hilton Hotel, New Orleans, LA. Registration will be open on Monday, October 15, from 8:00 AM to 8:00 PM, and daily thereafter. The APS Refresher Course, "Some Aspects of Exercise Physiology," is scheduled for Monday October 15, 1979 and will be hosted by Dr. E.S. Buskirk. Scientific sessions are scheduled Tuesday, October 16, through Friday, October 19. The APS Office and Council room will be located in the Newberry and Ascot Parlors on the third floor of the New Orleans Hilton.

TUTORIAL LECTURES:

I. Tuesday AM, October 16. Intro. by J.P. FILKINS. (1) Metabolic and Endocrine Alterations in Shock, J.A. SPITZER. (2) Endogenous Pyrogen Control, W. BEISEL. (3) Substance P, S. LEEMAN.

II. Tuesday PM, October 16. Intro. by R.F. LOWE. (1) Hormones and Hypertension, R.E. McCAA. (2) Advances in Hypertension, E.D. FROLICH. (3) Long Term Changes in Vascular Wall Function, H.V. SPARKS.

III. Wednesday AM, October 17. Intro. by M.G. LEVITZKY. (1) Neural Control of Cerebral Blood Flow, D.D. HEISTAD. (2) Local Control of Cerebral Blood Flow, R.M. BERNE. (3) Biotelemetry and Animal Models in the Study of Regulation of Ventilation, M.J. EVANICH.

IV. Wednesday PM, October 17. Intro. by H.I. MILLER. (1) Ammonium Metabolism, L. GOLDSTEIN. (2) Avian Renal Function, E. BRAUN. (3) Hyperbaric Physiology, B.A. HILLS.

V. Thursday AM, October 18. Intro. by J.C. PISANO. (1) Lipoprotein Metabolism, P.S. ROHEIM. (2) Adipocytes, Aging, and Cholesterol Metabolism, A.D. HARTMAN.

VI. Thursday PM, October 18. Intro. by T.P. SCHILB. (1) The Anomalous Osmotic Behavior of Human Red Cells, A.K. SOLOMON. (2)) Transport in Different Cell Series (Erythroid, Myloid, and Lymphoid), W.C. WISE. (3) Reference Phase Analysis of Intracellular Electrolyte and Water Activities, S. HOROWITZ.

VII. Friday AM, October 19. Intro. by N.R. KREISMAN. (1) Introduction of Physiology as a Professional Discipline into American Schools, H. DAVENPORT.

SYMPOSIUMS:

AM - Lymphatic Function, Pore Size and Permeability (Tribute to H.S. Mayerson). Session I, Chairman, A.E. TAYLOR.

PM - Session II, Chairman, J.M. DIANA.

AM - Aging (Co-sponsored by the Biosciences Section, Gerontological Society). Chairman, E.J. MASORO.

PM - Procedural Approaches to Gravitational Physiology (Sponsored by the IUBS Commission on Gravitational Physiology). Chairmen, X.J. MUSACCHIA and T.W. HALSTEAD.

Wednesday, October 17:

AM - Use of Ionophores and Antibiotics in Studies of Epithelia. Chairman, S.A. LEWIS.

AM - Respiratory Cardiovascular Interaction. Chairmen, S. PERMUTT and H.O. STINNETT.

PM - Tissue Oxygen Consumption and Vascular Resistance. Chairman, E.L. BOCKMAN.

Thursday, October 18:

AM - Vascular Influences of Prostaglandins. Chairman, L.P. FEIGEN.

PM - Calcium Regulatory Mechanisms in Vascular Smooth Muscle. Chairman, R.S. MURPHY.

Friday, October 19:

AM - Protein and Fat Metabolism in Carnivores and Hibernators. Chairman, G.E. FOLK, Jr.

BOWDITCH LECTURE: Tuesday, October 16, 4:30 PM:
Electrophysical Events Which Regulate Cellular and Molecular Events of Gastrointestinal Smooth Muscle. J.H. SZURSZEWSKI.

1979 ALBION O. BERNSTEIN AWARD

The Medical Society of the State of New York is accepting nominations for the 1979 Albion O. Bernstein, M.D. Award. This national award is given to a physician, surgeon, or scientist who has recently made a beneficial discovery in medicine, surgery, or the prevention of disease. Recent winners include Rosalyn S. Yalow, Ph.D., Solomon A. Berson, M.D., Baruch S. Blumberg, M.D., Ph.D., Manfred M. Mayer, Ph.D., Joseph L. Goldstein, M.D., Michael S. Brown, M.D., and Stanley Cohen, Ph.D.

The $2,000 award and appropriate scroll will be presented at the annual convention of the Medical Society of the State of New York, September 16-20, 1979. This award was endowed by the late Morris J. Bernstein in memory of his son, a physician who died in an accident while answering a hospital call in November 1940.

Nominators are asked to submit names on an official nomination form, available on request. Information submitted must include the nominee's curriculum vitae, a brief synopsis of the significance of the achievement and a list of publications or other contributions. Th deadline for nominations is August 1, 1979. Please submit to:

Bernstein Awards Committee
Medical Society of the State of New York
420 Lakeville Road
Lake Success, NY 11042

JOURNAL CHANGES - 1980

Two important new events in the publications program of the American Physiological Society will occur in 1980:

1. When the journals of the American Physiological Society were reorganized in 1976-77 much thought was given to the proper grouping of specialties in each journal. One of the combinations, endocrinology, metabolism, and gastrointestinal physiology, was a traditional one and gave the necessary size for a separate monthly journal. The resulting *American Journal of Physiology: Endocrinology, Metabolism and Gastrointestinal Physiology* has attracted articles of excellence in those areas. It has also grown in size. The journal is now of sufficient strength and size to warrant its separation into two individual monthly publications. The Publications Committee believes this separation will better serve the needs of physiologists. Therefore it is pleased to announce that in January 1980 the Society will begin to publish the:

American Journal of Physiology: Endocrinology and Metabolism,
edited by Ernst Knobil
and the
American Journal of Physiology: Gastrointestinal and Liver Physiology,,
edited by Leonard R. Johnson

These journals will succeed the *American Journal of Physiology: Endocrinology, Metabolism and Gastrointestinal Physiology,* which was so ably carried through the initial reorganization period by Rachmiel Levine.

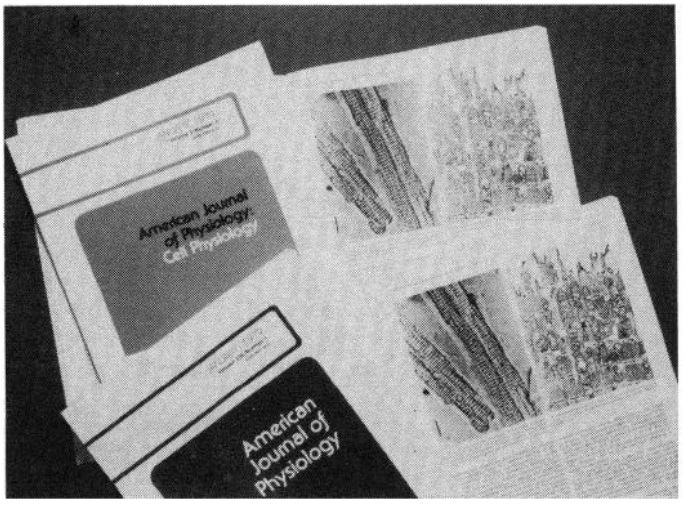
After July 1, 1979 authors should designate the specific journal to which they are submitting a new manuscript within the area of endocrinology, metabolism, and gastrointestinal physiology, as the new editors and editorial boards will be responsible for their evaluation.

2. Beginning in January, 1980, the *Journal of Neurophysiology* will be issued at monthly intervals, rather than at bimonthly intervals as in the past. The primary reason for this change is a continued growth in the number of manuscripts received by and published in the journal. One benefit to authors which will result from this change will be a reduction in the average interval between submission and publication of articles.

The Editorial Board of the *Journal of Neurophysiology* takes this occasion to remind its readers that it welcomes not only articles of the customary length but also short articles. While short articles are reviewed in the same fashion as papers of more traditional length, we would point out that the time required for reviewing and revising short articles is much less than for longer articles. Therefore, the turn-around time for short articles in the *Journal of Neurophysiology* issued monthly is certain to be substantially less that the present average.

Publications Committee

A.P. Fishman, *Chairman*
R.W. Berliner
R.M. Berne



HELP WANTED!!

The Publications Committee invites the help of the Members of the American Physiological Society in unriddling an apparently unsolvable problem.

Presently the same page numbers are used in the consolidated *American Journal of Physiology* and its individual journals. However, different journal title, volume, and issue number exists for each form of the journal. As most libraries continue to subscribe to the consolidated AJP and a growing number of individuals subscribe to the individual journals, proper citation should include both forms, e.g., *Am. J. Physiol.* 236(3): C103-C110, 1979 and *Am. J. Physiol.: Cell Physiol.* 5(2): C103-C110, 1979. This is cumbersome, but without both forms of the citation, it is troublesome to go directly to the reference.

The above is the method being used in the dual journals. Do you have a better solution to the problem? The reward for solving this problem will be threefold: 1) a one-year subscription to one of the journals of the American Physiological Society, 2) the everlasting gratitude of the Publications Committee, and 3) the elimination of another barrier to effective communication in science.

Please address queries and suggestions to:

Dr. A.P. Fishman, Publications Committee
American Physiological Society
9650 Rockville Pike
Bethesda, Maryland 20014

MEMBER SUBSCRIBERS TO JOURNALS

Dear Colleague:

Each of the individual journals of the *American Journal of Physiology* now has more subscribers than at the end of 1978. We are particularly pleased with the number of members who subscribe to one or more of the journals. We hope that soon all members will have joined these ranks.

Sincerely,
A.P. Fishman, Chairman
Publications Committee

BASIC RESEARCH
1980 INVESTMENTS IN THE FUTURE
A Joint Statement to the Congress
April 17, 1979

The 40 undersigned organizations and leaders of the nation's universities, colleges, research scientists, and engineers urge the Congress to support the principles of stable, balanced, and controlled investment in federal basic research programs as they are represented in the FY 1980 budget proposals for these programs in the National Science Foundation and in several mission agencies. We also urge Congress to insure funding levels for the research programs of the National Institutes of Health (NIH) consistent with the principles of stable, balanced, and controlled growth. We do so for the following reasons:

The nation's investments in basic research have produced a rich legacy for our country and for the world. The search for knowledge has brought many achievements: the elimination or control of dread diseases, such as poliomyelitis and tuberculosis; improved prevention and treatment of mental and behavioral problems, such as mental retardation and alcholism; technology of momentous economic and social importance, such as the transistor, the computer, and the laser; discovery of new materials; revolutions in the production of food; and development of the education and advanced training programs that are the very foundation for progress.

In the late 1960's and early 1970s, the nation experienced a long period of decline in real dollars in the level of investment for long-term basic science. In the search for quick solutions to pressing problems, funding policies sought immediate answers at the expense of stable, predictable support for the pursuit of knowledge. Now it is time to renew the nation's commitment to excellence in basic research.

We commend the Administration for proposing a broad strategy designed to produce sustaining and balanced national policies for advancing science and technology. The FY 1980 budget proposals for the National Science Foundation and for several mission agencies are important and necessary steps toward a controlled, coherent investment policy for the nation that would help to regain momentum in the search for new ideas, for new knowledge, and for solutions to the economic, technological, and social problems that confront our society. We need to know more if we are to maintain our economic growth, stimulate productivity, reduce inflation, promote our international competitiveness, protect our environment, meet energy demands, improve health, advance education, and guarantee national security. We do not currently have the knowledge base to meet these long-range objectives. Sustained national investment in the development of new knowledge and highly trained people is essential if our nation is to retain world leadership in science and technology. There must be balanced, sustained support for fundamental research across all fields of science to meet these challenges.

The basic research budgets for the National Science Foundation, in combination with the ones proposed for many mission agencies, are important starts; but they may barely sustain the nation's research enterprise at current levels. It should be pointed out that a government-wide increase of only about nine percent is proposed for basic research and that inflation has substantially increased since the President's budget was proposed. If the broad investment strategy now proposed by the President is adopted by the Congress and continued and protected in future years, that foundation of new knowledge which the nation needs to meet the challenges of the 1980's and 1990's can be built.

In one critical research agency, the National Institutes of Health (NIH), the budget fails to provide for needed stability. The funding recommendations for NIH research programs would result in cutting in half the number of new basic research awards to university-based and other researchers. Such sharp cuts would terminate promising programs, disrupt the research careers of highly talented young investigators, and discourage others from pursuing such careers. We urge Congress to insure stability for NIH research programs consistent with the government-wide investment strategy of sustained, balanced, and controlled growth.

The effectiveness of federal basic research programs is measured not only by their size, but also by the quality of the tools they provide to researchers and by the effectiveness of agency policies, procedures, and priorities in promoting flexiblity, innovation, and the willingness to take risks. The 1980 investment strategy would help stimulate research productivity by beginning to replace and upgrade the aging instrumentation and equipment in our research laboratories.

We also commend the Administration for its commitment to keep research productivity from being further compromised by excessive and unreasonable record keeping and reporting burdens which damage the research environment. We urge the Congress to help insure that administrative requirements are carefully formulated, and simplified wherever possible, so that the fundamental purpose of the federal investment, productive research, is not lost in the pursuit of ever more precise management.

Our national investment strategy must maintain and protect a balanced research structure in which universities, industry, and government all play a part. Government funding and regulatory policies sholuld safeguard the freedom of each sector, encouraging it to perform those roles particularly suited to it. Ways further to improve joint research activities between universities and industry should also be encouraged.

The APS Council agreed to endorse this statement at its April Meeting as one of 21 societies, associations and committees sponsoring the statement.

RESEARCH OPPORTUNITIES OFFERED
BY LEUKEMIA SOCIETY OF AMERICA

The Leukemia Society of America, Inc. is now accepting applications for grants to support research in the fields of leukemia and related disorders.

As an important source of funding for individual investigators whose work is concentrated on uncovering the cause or cure for leukemia, the lymphomas and Hodgkin's disease, the national voluntary agency offers three types of awards. According to Dr. Kenneth McCredie, its vice president for Medical and Scientific Affairs, the grants are intended to encourage studies at both the basic science and clinical levels.

Five-year scholarships for a total of $100,000 are available for researchers who have demonstrated their ability to conduct original investigations in the specified fields. Two-year special fellowships and fellowships for $31,000 and $25,000, respectively, are offered for those in the intermediate and entry stages of career development. In all categories, Dr. McCredie said, candidates must hold a doctoral degree but may not have attained the tenured status of associate professor. There are no restrictions as to age, citizenship, race, religion or sex.

Deadline for filing applications is Sept. 1, 1979, a month earlier than previously due to the increase in the number of proposals received last year and the extra time involved in reviewing them. Only one application in the scholar and special fellow categories will be accepted from a prospective sponsoring organization, although duplicates are permitted for fellows.

Project proposals will be evaluated on a competitive basis by the Society's volunteer Medical and Scientific Advisory Committee, nineteen specialists who also serve on the agency's National Board of Trustees. The reviews will take place next January with funding to start July 1, 1980.

Application forms and further information may be obtained by writing Dr. Kenneth McCredie, Vice President for Medical and Scientific Affairs, Leukemia Society of America, Inc., 211 East 43rd St., New York, NY. 10017.

FOUNDATIONS' FUND FELLOWSHIPS FOR SABBATICAL RESEARCH IN PSYCHIATRY AND ITS BASIC SCIENCES

The Foundations' Fund for Research in Psychiatry conducts a limited program of support for scholars on sabbaticl leave in order to further their research and contribute to the knowledge of psychiatric diagnosis, treatment, and prevention. The sabbatical must be spent away from the home institution at an internationally recognized institution.

Applications are open to recognized and creative investigators with demonstrated research contributions in the field who hold full-time positions in professional schools and graduate departments of universities or equivalent institutes of research. Applicants must be U.S. or Canadian citizens or permanent residents of the U.S. or Canada.

The deadline for receipt of applications is August 1, 1979 for sabbaticals beginning July 1, 1980 or later.

Information may be obtained from:

Foundations's Fund for Research in Psychiatry
100 York Street
New Haven, CT 06511

MAURICE B. VISSCHER
A HALF CENTURY AS A SCIENTIST—CITIZEN

A PAST PRESIDENTIAL ADDRESS UPDATE

About a year ago the Executive Secretary of our Society, who is also editor of this journal, wrote me saying that he would like to have a kind of update of the past presidential addresses of former Presidents of the APS. I presume he meant from those whose stints of service as chief officer of the Society were far enough in the past so that what they had said in their past presidential addresses whould have been long forgotten. I presume he also had in mind to obtain such updates from as many past presidents as possible before their numbers had been too greatly depleted by the ravages of time. I refer of course not only to their possible decease, but also to the need for some haste in order to obtain useful memoirs from them before too much deterioration had occurred in what my be called their neuropsychological capacity.

In rereading what I said on September 16, 1949 in my Past Presidential Address[1] at the second fall meeting of the APS in Augusta, Georgia, I note that I was very much exercised by the threats to civil liberties then posed by the House of Representatives Committee on Unamerican Activities and similar developments in the United States Senate. There is much more to be told in connection with related problems.

It happened that about a year before I was elected President of the APS I had introduced a resolution in the Council of the American Association for the Advancement of Science calling for the appointment of a Committee on Civil Liberties for Scientists. Such a committee was appointed and I was made its chairman. The committee had a number of meetings and was very fortunate in the fact that one of its members, a political scientist, was at the same time working on a more general study of civil liberties as they were being endangered by the Loyalty and Security Executive Order of 1947 by President Harry S. Truman, which he had issued in order to "prove that the Democratic Party was more anti-Communist than the Republicans," as one U.S. Senator told me. The Truman Executive Order required that all persons employed in any capacity by a Federal Government Department had to be cleared as to loyalty and security.

It might be noted that my "employment" by the Federal Security Agency was as a member of the first study section set up to advise concerning the quality of research grant applications for funds appropriated by Congress for cardiovascular research. As I recall, I spent perhaps two days a month quarterly for which I received a modest per diem. I do not have records, but I believe it was something like $25 per day.

The fact that I was, so to speak, picked on by the Loyalty Board of the federal agency was perhaps not too surprising. The year before, I had served as chairman of the Special Committee on the Civil Liberties of Scientists set up by the AAAS. The other members of the Committee were Professor Philip Bard of Johns Hopkins, Richard E. Cushman, Professor of Political Science at Cornell University in Ithica, Dr. Richard L. Meier, Executive Secretary of the Federation of American Scientists, and Dr. James R. Newman, a mathematician. The major consultant for the Committee was Professor Walter Gellhorn.

Professor Cushman had applied for and received a significant grant from the Rockefeller Foundation for the support of studies of the general effect of the Truman Loyalty-Security Order. He had already induced Professor Walter Gellhorn to serve as his major assistant with this study and he arranged that the first element in this study should be its application to the entire scientific community. As a matter of fact, the report of the committee of the AAAS was really prepared almost entirely by Walter Gellhorn with very little help, except general guidance, from the AAAS committee. This assignment to Walter Gellhorn undoubtedly influenced much of his later life because he became a nationally recognized knowledgeable expert in the whole matter of the impact of the 1947 Truman order on civil liberties.

The committee report was presented to the executive committee of the Council of the AAAS along with a much condensed summary of its findings. To our chagrin and really great surprise, the executive committee voted not to publish the report in the form in which we had submitted it. Since I was not a member of the executive committee I inquired as to what the objections to the report were. I ascertained that it was because of objections raised by a few representatives of industry, particularly oil geology, on the committee, that the decision to defer action was taken. I was asked, as chairman of the Special Committee, to meet with a neutral member of the new committee to work out some mutually agreeable compromise statement. The executive committee appointed the late Dr. E.C. Stakman who was then professor of plant pathology in my own university. I have forgotten much of the details of the discussion that followed, but recall quite vividly that Stakman was not really much impressed with the validity of the objections to our report. The report was made available in mimeographed form to any AAAS member requesting it in virtually its original form. The episode is worth recording nevertheless, because it demonstrates that the attitudes of the House Committee on Unamerican Activities and Senator Joseph McCarthy and Richard Nixon were shared by some members of the scientific community. The report of the AAAS Committee on Civil Liberties for Scientists was very clear in pointing out that the evidence for breaches of security or absence of loyalty on the part of members of the scientific community was practically nonexistent.

The Truman Loyalty Order had, however, a rather traumatic effect on me personally. Quite obviously I had been accused of disloyalty by someone, because in 1948 I received an official "interrogatory" from the chairman of the Loyalty Board of the Federal Security Agency, which included the National Institutes of Health. Oveta Culp Hobby was the Director.

I was asked to fill out a long and detailed statement with respect to my associations with dozens of people. There were two groups of people whom the Loyalty Board specialized on and the sort of questions that I was being asked indicated that the interrogatory sent to me was a kind of "fishing expedition" to get information about other people. This was obviously the technique used by the House Committee on Unamerican Activities and by Joe McCarthy and Richard Nixon. The two groups were the Unitarian Service Committee and the American Association of

[1]Musings of a Physiologist. American Journal of Physiology, 159:556-560, December, 1949.

Scientific Workers. As far as the Unitarian Service Committee is concerned, I had been a member of its Board of Directors and had been responsible for that committee's program of medical projects after World War Two. I was the scientific co-director of the Italian Medical Nutrition Mission in 1945 which was carried on in cooperation with the United Nations Relief and Rehabilitation Administration. I was also the Chairman of the Medical Teaching Mission to Austria conducted in cooperation with the World Health Organization in 1947.

These medical missions were carried on by the Unitarian Service Committee because it was felt, and I had encouraged the committee to devote itself to such activities, that the Service Committee could perform the greatest service by recruiting the volunteer cooperation of some of the most distinguished American scientists in these missions.

Although I did not participate in them myself as a member, the Service Committee also sent missions to Czechoslovakia, Germany, Japan, and some other countries. At the time this program was in operation, the academic medical people in these countries were suffering from very real isolation from medical science and scientists in the Western world.

Nevertheless, in connection with this Service Committee activity, I happened to meet a few people engaged in other activities for the Unitarian Service Committee whom the military intelligence community had come to suspect as "communist sympathizers." I was asked specific questions about these people and actually was unable to verify any of the implied accusations because in my association with these people we had never discussed such things as US – Soviet relations. It may be of interest to note that several names that were mentioned in the interrogatory were of persons whom I had never met and actually did not know anything about. This is one of my reasons for saying that the interrogatory itself was a fishing expedition because neither the FBI nor the army intellignece could have obtained any information linking me in any way with those people.

The fact that the loyalty agency thought that my connections with the American Association of Scientific Workers merited inquiry is really not quite so surprising because there had been a scandal involving the Canadian Association of Scientific Workers and it was well known that the Frenchman Joliot-Curie was probably himself an ideological communist and he was associated with the World Federation of Scientific Workers, with which the AASW had some connection. However, again I had never had any discussions with other members of the AASW with regard to relations with the USSR and had no basis for any assertion that I suspected any of them to be disloyal to the United States. One of the amusing aspects of this part of the interrogatory was that Edward U. Condon who was at that time director of the United States National Bureau of Standards and had already gone through several loyalty security checks, was a very active participant in the AASW action in connection with the setting up of the Committee on the Civil Liberties of Scientists. It is also of some interest that Condon was elected president of the AAAS in 1952, two years following the issuance of our committee report.

As I mentioned earlier, the Truman Loyalty Order had a traumatic effect on me personally. In 1948 I was informed by the Chief Security Officer of the University of Minnesota, Mr. C.B. Hanscombe, that my phones were being tapped and that, although he had no business telling me so, he wanted me to know. He also informed me that the University Regents had allowed him to permit federal agents, presumably the FBI, to enter any departmental office in the University and search all files in such offices for any material that might be of interest to them.

In the mood then current in the United States, there was little reason to hope that the public at large would object to the reasoning of a university governing body (a board of regents) giving authority to the FBI and military security to investigate the reliability of its staff members. I may have made a mistake in not at that time attempting to expose the facts, but I was under pressure not to do so. First of all, the information I had received from the University's own officer was given confidentially and at that time it would have led to serious consequences for him if I had quoted him. Incidentally, I should add that he is dead and comfortably in his grave now.

Another reason for not rocking the boat was that at this time the Minnesota Legislature was considering passage of an act which would have required the kind of certification of "non-disloyalty" on the part of its staff which had already been passed by several state legislatures. It happened that this bill was being held up in committee in the State Senate after it had been passed overwhelmingly in the House of Representatives. It was being held by the chairman, Senator Gerald Mullin, of the Senate Judiciary Committee, to which it had been referred. This senator was nominally a conservative, but actually was very friendly to the University and it was due to his action, really solely, that the Minnesota Legislature did not pass that stupid type of legislation.

After a very troubling six months I received the following letter, which I think I should make public, even though it was marked personal and confidential.

February 15, 1949 — Federal Security Agency
Washington, D.C.

Dear Dr. Visscher:

This is to inform you that this Board has determined, on the basis of the information before it, that no reasonable grounds exist for belief that you are disloyal to the Government of the United States.

The determination of this Board is subject to post-audit by the Loyalty Review Board on the record transmitted, with respect to matters of procedure and also to the right of the Loyalty Review Board to institute a review of the case on the merits. In event of a review of the case on its merits, you will be given a due opportunity to be heard.

Sincerely yours,
(signed)
Joseph E. McElvain
Chairman
Board of Inquiry on Employee Loyalty

This terminated my period of actue anxiety. However, it did not encourage me to believe that it would never happen again. So long as the great fear on the part of the federal government of outspoken liberals persisted, I should not expose myself by serving as a consultant to any federal agency. I also had to refuse such assignments as one as a consultant to the World Health Organization because the United States Department of State required that any U.S. national appointed to a UN specialized agency in any capacity had to go through State Department security-loyalty check. Since I had decided on principle not to expose myself to that kind of trauma again, I had to refuse a request to serve as an advisor to the All-India Institute of Medical Sciences in New Delhi.

This decision of mine not to allow myself to be in an exposed position again made it possible for me to be comfortable about participating in such programs as the Symposium on Social Responsibility in Science at the annual meeting of the AAAS in St. Louis, Missouri on December 30, 1952 where I read a paper which I entitled "On the Proper Role of Scientists in a Schizophrenic World." This was at the height of the Joe McCarthy period in the United States. This speech elicited nationwide attention. I was asked whether I would allow the publication of the speech in its entirety in the magazine The Nation, to which I agreed. Subsequently, I had an invitation, which I did not accept, to write a full length book on the subject of civil liberties for scientists by one of the well known scientific publishing houses.

There were some very amusing things that occurred to me personally in connection with the paranoid attitudes of United States officialdom during that period. In 1952 I became the Secretary General of the International Union of Physiological Sciences. In that capacity I informed the officers of each adhering society throughout the world as to what their dues were. They sent them to me and I forwarded them to the treasurer. One morning I received a telephone call from a very agitated person in the United States Post Office who said that I had a communication from the Academy of Sciences in the USSR. Obviously I must have been on the list of persons whose mail was being opened by the FBI because this person went on to say: "There is a check made out to you personally for a considerable amount of money from the Academy of Sciences of the USSR." He then asked: "Do you want me to send this to you or do you want to send it back because it may embarrass you to receive money from the USSR?" I recall having told him that although the check may have been made out to me it was intended to be the annual dues to the IUPS from the Academy of Sciences of the USSR and that it would not embarrass me at all to handle the check because I would see to it that it was deposited by the Treasurer of the IUPS in the account of the latter.

The paranoid attitudes of the federal agencies and actually of many other people did not end with the demise of Joe McCarthy. As a matter of fact, a major episode of the same sort occurred in connection with the International Physiological Congress and the business meeting of the IUPS in Buenos Aires in August, 1959. It happens that I had written a complete account of that fiasco shortly after the event in a letter than I sent to the late Senator and later Vice-President Hubert H. Humphrey on August 21, 1959. Because it conveys important information and something of the flavor of the situation, I am simply including here the text of the entire letter:

August 21, 1959

Senator Hubert H. Humphrey
Senate Office Building
Washington, D.C.

Dear Hubert:

I want to tell you for your own personal information (not for any wider dissemination at this time) what happened at the Buenos Aires Meeting of the International Union of Physiological Sciences. It is a story of a "tempest in a teapot (chinese)," but it will be good background information for you and I want advice. About two weeks before I left Minneapolis to attend this meeting I received a letter in my capacity as General Secretary of the Union from Professor A.C. Liu, Head of the Department of Biophysics at one of the Medical Schools in Taipei, Formosa, asking for admission to the Union (IUPS) of the newly reactivated Chinese Physiological Society. This Society used to be on the Mainland of China and most of the Chinese physiologists are of course now on the mainland. I wrote back saying that the Union needed more information concerning the Statutes of the Society and especially regarding the geographic area that it claimed to cover, realizing that this might become a "hot potato."

Upon my arrival in Buenos Aires on the afternoon of August 4, I was called by telephone in my Hotel by the Ambassador of the Republic of China, Dr. Shao-Hwa Tan, who wished to speak with me as soon as possible. He came over to the Hotel and over a glass of sherry he explained his interest in the above matter and I showed him all of the documents, which he had not seen. I also explained to him that International Scientific Unions were totally non-political and that as I understood the policy of IUPS it would not admit any Society which did not in fact contain in its membership the scientists of the area which it purported to cover. I told him that other Scientific Unions had had trouble over this issue before and that the more general view among scientists was that any bona fide group of scientists could join, but that such adherence was not to be under conditions which would prevent any other bona fide group of scientists from joining. I told him that the geographic claims of the Chinese Physiological Society were not spelled out and that the best thing to do under the circumstances seemed to me to be to defer any action at this meeting of the General Assembly of the Union.

Nevertheless he wished to talk to me again and invited me to dinner at the Embassy on August 7.

However in the meantime at noon on August 5, Mr. Birnbaum of the United States Embassy in Buenos Aires called me and said that "the Minister" wished to see me at 3 p.m. that day. At the Embassy I had a conference with Mr. Birnbaum, Mr. Nugent and one or two other persons whose names I did not get. I believe the Ambassador was not present. I presented them with all the documents for the General Assembly, which they had not seen. They had had instructions from Washington to contact me and to urge on me the desirability of having the Society from the Republic of China admitted for diplomatic reasons. I explained that the International Scientific Unions tried to avoid politics altogether and that our concern was solely to promote physiological science. It was pointed out to me what U.S. policy regarding the two-China problem was, which I told them I knew quite well and realized that there were very great problems. I was asked whether the American Physiological Society got appropriations from Congress, with the explicit statement that to fail to follow the Department of State suggestions might jeopardize such appropriations. I replied that we got no direct support from Congress.

The U.S. Delegation to the IUPS is not a State Department supported or appointed Delegation, but

rather was appointed by the National Academy of Sciences. Our Chairman, Dr. W.O. Fenn of the University of Rochester, was briefed by the Department of State before going to the meeting and was told only that the Department of State would look upon it with very great disfavor if any U.S. Delegate would vote *for* the admission of scientists from Red China. Dr. Wallace Brode who is the Science Advisor or Coordinator for the Secretary of State did the majority of the briefing, as I understand it. He did not mention the Republic of China--I surmize he did not even know that this question might come up.

On August 7 I had dinner with Dr. Tan, Dr. Liu, Mr. Nugent and about 10 other people, and talked at some length privately with Drs. Tan and Liu. I asked specifically whether the application could come under a geographic rather than a governmental name, because I said I was sure there would be serious trouble in getting the Council and the Assembly to accept a Society claiming to cover all of China. I suggested the "Physiological Society of Taiwan." This was not acceptable. I told them I would present the case as sympathetically as possible but that I doubted it would be acceptable to call their Society that of the Republic of China because of the political nature of the issues raised since we were politically neutral, and had to be if we did not intend to destroy the International Union. I told them that the USSR and her satellite groups would undoubtedly make a great noise over this issue and that I did not believe the U.S. Delegation could possibly muster enough support to accomplish the election of the Formosa group as the Republic of China Society, even if we were disposed to try to force it. I said I thought that tabling the matter for the present was preferable from every viewpoint. No one would be turned down and time would be allowed to work out a satisfactory arrangement for both groups of scientists to join IUPS.

The U.S. Delegation met on August 9 before the Council Meeting in Buenos Aires. I explained the problem and they were of the unanimous opinion that deferral of action was the action of choice. Besides Dr. Fenn and me, the Delegation included Dr. Carl Schmidt, University of Pennsylvania, Dr. K.K. Chen, Eli Lilly and Company and Dr. V.W. Wulff, Syracuse University. In addition Dr. R.F. Pitts, President of the American Physiological Society was present and concurred.

At the Council and General Assembly meetings the action I anticipated was taken unanimously.

On August 14 at about 3:30 P.M. Mr. Nugent of the U.S. Embassy found me at the Congress meetings and said that they had had urgent instructions from Washington to ask the U.S. Delegation for a reconsideration of this matter by requesting a Special Session of the General Assembly of IUPS (some 40 plus people from 20 countries) before the Congress ended the next day at noon.

I told him he should see Dr. Fenn, who was chairman of the U.S. Delegation, but who was at that time the Chairman of a scientific session, which was to go on until 5:30 P.M. He spoke with Dr. Fenn later, who agreed to ask whether such a Session was possible but told him it was very unlikely. Dr. Fenn consulted the 1956-9 President, Professor Heymans of Belgium, who said it was totally impossible, and who was in fact very much irritated by the intrusion of the U.S. Department of State into the matter.

I am telling you this story in full detail because I think it is fantastic and demonstrates a lack of good judgment of the part of our State Department which is damaging to the reputation of our country. The provision of information to U.S. scientists representing their scientific disciplines in the U.S. on international bodies is perfectly correct. We should know what the U.S. official views are. For the most part we know them quite well ourselves but I have no objection to "getting it straight from the horse's mouth." However, when it comes to asking us to do things that make the U.S. appear ridiculous in the eyes of 3000 top scientists from all over the world I call a halt. To ask us to have a Special Session of a General Assembly called in order to promote a specific diplomatic interest at a moment's notice on the last day of a meeting is so ridiculous that one would imagine that no one would contemplate it. Obviously there are people in the Department of State with little enough sense of balance to do so because it was done, and worst of all they pushed us into publicly acknowledging that we were asked to do so. It became obvious to scientists from many nations that the U.S. was trying to fight the cold war through its scientific bodies.

I am frankly very much disappointed, disillusioned and on the verge of being disgusted.

We on the U.S. Delegation felt that we were protecting U.S. interests best by avoiding any open controversy. We also felt that as scientists we could not play national politics. Science and political ideology and strategy do not mix. We must either give up the idea of international scientific cooperation or the Department of State must get out of trying to direct U.S. scientists in matters like this.

I want your advice. What should we do about this sort of meddling?

Sincerely,

(signed)
Maurice B. Visscher

I was very much disappointed that Senator Humphrey did not respond in any way to this letter. Actually I had had a good deal to do with him during his earlier political campaigns. It happens that I chaired a political meeting of students and staff at the time of Hubert Humphrey's first unsuccessful campaign for the mayoralty of Minneapolis and had been one of his active supporters in his subsequent political campaigns, including those for the senatorship from Minnesota. Humphrey had been very complimentary initially with respect to my civil liberties activities, including a letter dated January 19, 1953 in response to my sending him a copy of the speech I gave on December 30, 1952 in St. Louis, which was, in fact, a slashing attack on the House Unamerican Activities Committee and the McCarthy-Nixon ap-

proach. At this time, Humphrey said "Articles such as yours are an absolute must. The tragedy is that too many media of public opinion are already shut off to efforts such as yours. Keep up the good work. I will do my best on this front." However, Humphrey's attitude changed in the next few years. He became a co-sponsor of the seriously repressive McCarran Act and, of course, later became one of those Democrats in Congress who came to believe that the Democrats needed to become more anti-communist than the Republicans if they were to survive.

Perhaps my younger colleagues may be interested in other activities of a public service nature in which I have been engaged. In July 1957 I was appointed by the then Governor of Minnesota, Orville L. Freeman, as a member of his Committee on Atomic Energy Development Problems. The chairman of that committee was Lee Loevinger. He became later a member of the Federal Communications Commission. I was asked to be chairman of the subcommittee on the biological effects of ionizing radiation. I was asked to serve on this Governor's committee because I was among the relatively few biomedical scientists in the state who had any practical experience with the use of radioisotopes. Other biologists who were appointed were Richard Caldecott, now Dean of the College of Biological Sciences at the University of Minnesota, and William O. Caster, who left Minnesota to go to the University of Georgia as Professor of Nutrition. There were, in addition, physicists and engineers and representatives of the general public. The committee took a very broad view of its assignment and looked very carefully into the hazards as well as the possible utility of atomic energy in the State of Minnesota. A special task force looked into the background radiation from fall-out from the bomb testing program that had been going on for several years at the Nevada test site. One of the studies carried on at the University of Minnesota in the Department of Agricuture was a study of the Beta radioactivity of grain from the Plains States reaching the Minneapolis market. The very high Beta activity measured was, I believe, the first indication of the fact that major supplies of United States grain exceeded the maximum permissable level of the radioactive isotope presumably responsible for the high level--namely, Strontium 90. Because the committee felt that analyses performed by the laboratories of the Atomic Energy Commission would be more readily accepted, the committee sent samples of 1956, 1957, and 1958 wheat from eight Minnesota locations to the AEC laboratories for analysis. In general, 1956 samples were below the then current maximum permissable level. But the 1957 and 1958 samples were all above that level. On behalf of the Minnesota Governor's Committee I presented testimony before the Subcommittee of Fallout Problems of the joint Congressional Committee on Atomic Energy on May 4, 1959. Rereading that testimony reminds me that I told the Congressional committee that it seemed to us that the changes that had just been made by the National Committee on Radiation Protection, raising the maximum permissable dose for Sr-90 in food, was absurd, and I called the raising of the maximum permissable body burden for Sr-90 "astoundingly brash because the facts regarding human damage from low doses of Sr-90 will not be known for another ten to twenty years." In 1959 we were objecting to the "playing-down" of the potential hazards of low-level radioactivity by the NCRP. The Minnesota Governor's Committee was undoubtedly responsible for stimulating a great deal of general opposition to the atmospheric testing of thermonuclear bombs.

When the National Committee for a Sane Nuclear Policy was formed I was asked to become one of its National Sponsors, which I gladly agreed to do because I saw clearly that thermonuclear war was simply reciprocal genocide and serious preparation for it was an evidence of a kind of mass insanity. I later became a member of its National Board of Directors, serving for about ten years, until I became so much involved in the anti-Vietnam War movement that I felt obliged to give up some other activities. In 1968 I became convinced that the U.S. was engaged in an irrational, counter-productive and inhumane venture in its Vietnam War. With a group of like-minded persons I helped form and became the chairman of Minnesotans to End the War in Vietnam. We organized what we called the BiPartisan Caucus, consisting of prominent Republicans and Democrats in the State who shared the conviction that the Vietnam War was both immoral and counter-productive. The BiPartisan Caucus organized the first and only major antiwar mass rally in Minnesota with the theme "Dump the War," held in the Minnesota Sports Center. The overflow rally was addressed by nationally prominent Republicans and Democrats and was responsible for creating a broad-based opposition to continuation of the War in the community. It certainly did not contribute to intra-party unity in Minnesota, because in this State Eugene McCarthy, then its senior U.S. Senator, was a serious contender for the Presidential nomination by the Democratic Party. Although the support for Vice-President Hubert H. Humphrey had been considerably eroded by his pro-war stance, there were many of the Party faithful who were convinced, wrongly so it turned out, that he could be counted on to defeat Richard Nixon. The 1968 Democratic Convention in Chicago was extremely traumatic and Hubert Humphrey's failure to repudiate Lyndon Johnson's disastrous as well as deceptive and immoral S.E. Asia policy set the stage for his defeat by Richard Nixon, which in turn proved to be one of the greatest catastrophies in U.S. history. In a small way Minnesotans to End the War in Vietnam had helped precipitate the repudiation of the Vietnam War.

My own participation in the Anti-War Movement was an outgrowth of my earlier activities in the civil liberties battle, my activities on the international scene for the IUPS and the Unitarian Service Committee medical science contributions, and my work in the Minnesota Governor's Committee on Atomic Energy Problems. Although in many cases there were short-term disappointments and disillusionments, as I look back I feel rewarded for having played a meaningful role in the long-term successes in maintaining civil liberties, in arousing justified concern about ionizing radiation hazards, and in a rational skepticism about the possibility of survival in a military climate that envisions reciprocal genocide in a thermonuclear holocaust as a "viable" option.

I should not, however, fail to mention the fact that my service in various capacities to the American Physiological Society ultimately involved me in many other related activities. After serving as a Council member, as the last elected Secretary, and the President of the Society I was appointed as member of the Board of Publication Control which managed the several publications of the Society. One of the serious problems that the Society had during the early 1950's was lack of adequate space, particularly for the editorial work on the journals. Dr. Milton Lee, then Executive Secretary of the APS and Managing Editor of the publications encouraged the Board of Publication Trustees to find a suitable home for the Society and its journals. Dr. William F. Hamilton made an energetic effort to find suitable places in the Washington area and located a beautiful house and eleven acre tract of land at 9650 Rockville Pike on the outskirts of Bethesda. The APS had been housed with the National Academy of Sciences, 2101 Constitution Avenue, in Washington. Milton Lee was very much pleased with the prospect of moving to Bethesda. Dr. Wallace Fenn, the Chairman of the Board, was unwilling to

see the Board of Publication Trustees purchase the property on its own authority and therefore the officers of the Society were also brough into the discussion. The property was purchased and was officially called Beaumont House. After its puchase by the Board of Trustees it was decided to offer it to the FASEB with the stipulation that if any parts other than the house and its immediate grounds were sold for residential development the BPT of the Society should be reimbursed to the extent of its investment in the purchase. Actually, within a few years enough of the undeveloped tract was sold to cover the cost of the entire acquisition. In other words, Bill Hamilton's prediction that the values of property in the Washington suburb area were bound to increase turned out to be completely correct.

Although as the third member of the BPT I was able to give Hamilton and Lee considerable help in the purchase of Beaumont House, perhaps my most significant contribution as a member of that Board was the initiation of the Handbook of Physiology series which the Society has sponsored. This was initiated because we on the Board believed that it was important to have available, especially to graduate students in physiology but also for anyone wishing to obtain reliable information in any field of physiology, a handbook which would be revised at least every ten years.

My service in relation to publications stimulated my interest in the entire abstracting and indexing process and I served for several terms on the Board of Directors of Biological Abstracts and for one term as its President. Also because of these interests I was asked to serve on the Board of Directors of Annual Reviews, Inc. Initially the annual Review of Physiology was a kind of joint venture between the American Physiological Society and the Annual Reviews organization in Palo Alto. At that time Dr. Murray Luck was the Editor of the Annual Review of Biochemistry. He approached our Society about initiating an Annual Review of Physiology. There was some reluctance because it was feared that the role of Physiological Reviews might be preempted by an Annual Review publication. As it has turned out there has not been serious competition, although the entire problem of the role of scientific reviews of various types is still today in as great a state of flux as it was thirty years ago. During the time that I served as a member of the Board of Directors of Annual Reviews, Inc. it has greatly expanded its coverage in the scientific field. It now covers twenty-two separate fields of science. It has continued to provide a great deal of information in reviews that cover the most active fields of research in each general science, but it no longer makes a serious pretense of providing references and discussion of contributions in all areas of a general science on an annual basis. The earler criticism of Annual Reviews--namely that it was, in essence, a kind of annotated bibliography--is therefore no longer valid. The Annual Reviews have, however, maintained their policy of providing large coverage at very low cost per volume. This it is able to do because its Board of Directors serves without compensation and authors serve without compensation, while the working editors of volumes are compensated very modestly. In other words, Annual Reviews operates much as a scientific society would operate in financial matters.

Another type of interest and activity which engaged me from 1945 to the present is that of the National Society for Medical Research. This was the brainchild of one of our APS former presidents, Anton Julius Carlson. He proposed to the governing body of the Association of American Medical Colleges that it become a sponsor of an organization of as many biological and biomedical societies as it was possible to induce to join in an effort to promote the interests of biomedical research. In the first instance he had the very great assistance of Andrew Conway Ivy who had been one of his graduate students and became head of the Division of Physiology and Pharmacology at the Northwestern University Medical School. Carlson became President and Ivy the Secretary of the new organization--the National Society for Medical Research. Ivy was extremely influential in persuading a very large number of societies concerned with clinical investigation and biological societies employing animal experimentation to join the new organization.

Until Ivy, in a most uncharacteristic way, became involved as a proponent of krebiozen in the management of cancer patients he was one of the most prestigious basic scientists in clinical investigation. He was a member of the National Advisory Cancer Council. He had been Scientific Director of the Naval Medical Research Institute. He was a medical consultant to the Nuremburg Commission on War Crimes. I mention these activities of Andrew Ivy because in 1960 I received a long-distance telephone call one day from A.J. Carlson asking me whether I would be willing to serve as vice-president of the National Society for Medical Research. He said that it was very important to the survival of NSMR that there be some officer other than its current secretary who would take his place if he, A.J.C., were to be incapable of serving. He referred to the fact that he had been diagnosed as having a carcinoma of the prostate and, although he did not think that an early demise was very likely, he was tremendously concerned over the fact that Andrew Ivy was unalterably committed to the promotion of krebiozen as a cancer cure. I hesitated very seriously about saying yes, because I myself had a very friendly relationship with Dr. Ivy and because I knew that Ivy had played a very constructive role in the APS and FASEB activities over many years. However, I was also very anxious to assist Carlson in any way I could. I had a feeling of indebtedness to him because I had spent the better part of a year as a National Research Council Postdoctoral Medical Fellow in his laboratory thirty-four years earlier. Furthermore, like so many of his scientific colleagues, I had great respect for Carlson's humaneness and philosophical perspicacity. I knew that he would not be asking me to do this unless he was himself convinced that there was no way to dissuade Dr. Ivy from destroying his scientific reputation and prestige by clinging to the krebiozen myth.

In other words, krebiozen became indirectly the reason for my becoming President a few years later of the National Society for Medical Research.

I served as a President of the NSMR from 1966 to 1978. It fell to my lot to find additional funding to carry on the public information program which was necessary in order to preserve a viable legal environment for research involving the use of animals to continue. One person more than any other played a role in preserving the NSMR. That was Dr. Maurice L. Tainter, who had been Professor of Pharmacology at Stanford and became heavily involved in physiological and pharmacological research as Director of the Sterling-Winthrop Research Institute. He was very well known and highly respected in the pharmaceutical research community and was able to obtain generous support for the educational programs of the NSMR from industrial sources. This was made somewhat easier by the fact that donations to the NSMR were income-tax exempt by virtue of the charitable nature of its activities.

A book could be written about the details of the travails of the NSMR in opposing the passage by Congress of highly restrictive legislation. However, for the American Physiological Society, only one item is particularly interesting. It is the fact that one of our own members, now deceased--Robert Gesell, then Professor of Physiology at the University of Michigan--attempted to get the Society to pass a resolution asking that the United States Con-

gress pass an act comparable to the British Cruelty to Animals Act of Parliament of 1876. That episode and something about later developments I have described in an article that I wrote for this journal (Volume 6, Number 1, page 57, February, 1963). The fact is that Gesell's daughter Christine, now Mrs. Roger Stevens, is still a prime mover in attempts to get the U.S. Congress to pass ever more burdensome control legislation.

My reason for preparing this update of what I said and wrote thirty years ago is that I think it may be of some interest and encouragement to my younger colleagues to know that one can combine a productive scientific career with some service to the larger society in which we live in relation to problems of great human importance. I want to point out that no small part of the influence that I was able to exert in relation to more general problems was a result of the fact that I had already accomplished something in and was continuing to make significant contributions to the science of physiology. If I had not done and continued to do creative work in the fields of circulation, respiration, and material transport that had justified elections to the American Academy of Arts and Sciences, the National Academy of Sciences, and the American Philosophical Society I am sure that I would not have been able to exert influence of any importance in the citizenship field.

Thus, what I am actually saying after thirty years is, first of all, pay attention to your scientific creativity and productivity. But also remember that you live in a society as I have in which there are acute problems in which your scientific expertise may help society solve its problems and, perhaps not less important, in which the ethic of truthfulness which is at the heart of the scientific method may be infused into societal decisions.

I cannot finish this update without acknowledging my profound debt to my institutional colleagues and former graduate students, without whose intellectual stimulus and enthusiastic collaboration I could never have been as productive in scientific work and would not have been as enthusiastic in my citizenship.

SENIOR INTERNATIONAL FELLOWSHIPS

The Fogarty International Center, National Institutes of Health, announces Senior International Fellowships for outstanding mid-career faculty members of U.S. biomedical or graduate-level educational institutions to pursue research and study in the Health sciences at foreign host institutions. It is intended that these awards be career-enhancing and provide mutual benefit to both the U.S. and foreign institutions. Selection is on a competitive basis depending upon qualifications of the applicant, scientific merit of the proposed work, and benefit to be derived from the collaboration. Awards are made for periods of three to 12 months.

Applicants must be U.S. citizens or permanent residents, hold a fulltime appointment at a U.S. institution, and have at least five years' experience beyond the doctorate. Applications require nomination by the U.S. institution and invitation by a foreign institution. Transportation, allowance for the foreign institution,and an award of up to $24,000/per annum are provided. Deadline for annual receipt of applications is October 1 wi announcements of awards in March.

Special Emphasis Senior International Fellowships. A limited number of fellowships will be awarded in the special fields of *aging, arthritis, diabetes, epilepsy* and *tropical diseases.* These awards will be in addition to those of the regular program. Eligibility requirements and general terms are the same as for the regular Senior International Fellowships Program.

Concurrent applications to each program are not permitted.

For further information, write to:

Scholars and Fellowships
Program Branch
Fogarty International Center
NIH, Bethesda, MD 20205.

NEWS FROM SENIOR PHYSIOLOGISTS

Charles Hassett to Hallowell Davis:

I have contiued my work as a consultant to NIOSH (National Institute of Occupational Safety and Health) and have provided similar service to a local environmental engineering firm. My wife and I spend as much time as possible in Woods Hole on Cape Cod during the summer. These arrangements keep me in touch with professional matters but leave free time for personal interest. I recommend such a mixture for any retired members who are lucky enough to be able to achieve it.

Fred Benjamin to Hal:

I always read with interest the "Letters from Senior Physiologists" and hearing of their whereabouts and letting others know of our work in the Department of Transportation. I continue my work in the National Highway Traffic Safety Administration. I am involved in the problem of alcohol, drugs, and driving. We have in this country every year some 24,000 highway fatalities involving alcohol. In our headquarters office here in Washington, we do not do any research work, and the work we sponsor has to have direct application to the highway safety problem. In the eight years I have been with this Administration we have learned a lot, but we have not been successful so far as the reduction of alcohol or drug-involved accidents is concerned. This can be very frustrating, and we are always looking for new concepts and approaches to promote traffic safety.

Frank A. Brown, Jr. to Hy Mayerson:

I have read avidly all the letters from Senior Physiologists end enjoy learning what my retired colleagues are doing. After completing my doctorate at Harvard, I spent 42 years in two major midwestern Universities, 3 at the University of Illinois and 39 at Northwestern. Each summer I worked at the Woods Hole Marine Biological Lab. Compulsory retirement in our University is 68 which I reached by September 1976. The University generously permitted me to reduce and ultimately to abolish my participation in undergraduate teaching and to devote most of my time to seminars, my last doctoral candidates and my own research program. A continuing NSF grant enabled my to maintain an active laboratory for an additional year whereafter I moved into a small office in the university. A very bright doctoral student, my 40th, still hangs on.

I participate in relevant National and International meetings and symposia, accept visiting professorships and give invitational lectures dealing with the biological clock phenomenon, publish research articles based upon data obtained earlier, and prepare reviews and popular works. I was actively involved in the first Gordon Conference in Chronobiology this past summer in New Hampshire. It has been gratifying to see my long-time conviction and theme that living creatures are steadily interacting with their rhythmic physical environment, and with one another, through extremely feeble electromagnetic fields slowly but inexorably gaining ground and ushering in a new domain for scientific exploration.

Life is pleasant in retirement. We can move more freely among our three homes, in Wilmette, IL, Woods Hole, and Machiasport, Maine. My wife and I have more time to enjoy our three children, their spouses and 8 grandchildren who visit us from time to time especially summers in Woods Hole, where boating, fishing, swimming, bicycling, keeps everyone busy and happy. As for words of wisdom for younger colleagues, do not choose Physiology unless you really love it; if you do it is impossible to find a more exciting and satisfying life.

Edward J. Van Liere to Hy:

I am in reasonably good health and have a comfortable office in our Medical Center and work for five to six hours each day. I have just completed a manuscript, "100 Years of Physiology at West Virginia University - 1869-1969." It is now in the hands of the publisher and hopefully will be out this coming year. I came to West Virginia in 1921 so I am an old-timer indeed.

William M. Hart to Bruce Dill:

I will be relieved shortly as Department Chairman because of age. It is nice to have options open but it seems likely that I will continue on the staff here (Univ. of Missouri-Columbia) at least for the foreseeable future. My continued clinical interest in Neuroopthalmology is much in demand and I feel useful in seeing lots of patients. Teaching is still fun too.

Let me say that I am one of the foremost exponents for the value of coronary by-pass surgery. I had mine three years ago and since then I have been in better health than I was ten to fifteen years ago. Let us agree that we will exchange letters again in ten years.

Theodore Koppanyi to Edward Adolph:

I must report to you that I am well, working both in this country and abroad. I am actively engaged in research about antiarrhythmic drugs and clinical pharmacology of Parkinson disease. In addition, I am requested to write reviews on various subjects, e.g. on barbituates. We met at the Federation meetings for the first time in 1924 and I must say we were considerably younger and more ambitious. Alas, the youthfulness is gone but the ambition remains - a bad combination.

Otto G. Edholm to Edward:

A small book, "Man: Hot and Cold" by myself has just been published by Edward Arnold Ltd. in their series, Studies in Biology. I am continuing some research here (University College London) and also conduct some seminars on subjects such as thermal comfort to the advanced students in architecture. I can only say to younger colleagues that they may look forward to retirement when one is to a great extent, free to do what one wishes, and for physiologists what can be better than doing physiology?

Paul Sekelj to Edward:

I am in good health and participating, part-time in departmental activities at McGill. I hope to go on writing a few more papers, although with each work in preparation I feel a bit like a man who is about to withdraw his last savings from the bank. I have kept up my interests in antique furnitures and painting. I am doing work with water color, acrylic and oil. Last year three of my rather large size paintings were exhibited at the Saidi Bronfman Art Center. My free time is spent with my wife, and in the summer with our children and grandchildren in our country place at the beautiful Lake Memphremagog, just north of the Vermont border near to good ski areas. Downhill, crosscountry skiing and swimming are still my favorite sports. Best wishes to all active and retired members of APS.

Walter Redisch to Edward:

My tendencies not to add intellectual retirement to organizational facts are unchanged, but the realization of planned dreaming has become somewhat more ludicrous than before. My yearly European trip to give lectures in Austria, Germany and Czechoslovakia and collect some of their honor awards ended this year with illness. I am recovering and starting to pitch in again in my lifelong attempt to study the physiology of microcirculation and its intriguing relationships to the clinic of cardiovascular disease.

Arthur B. Otis to Horace Davenport:

I will be retiring soon as Chairman of the Department of Physiology at the University of Florida but I plan to remain as a Professor. I still do some work in the laboratory and have two graduate students who help me keep interested. I am on the editorial board of the *Journal of Applied Physiology* and of Respiration Physiology. Occasionally, I write a paper myself. I am becoming increasingly interested in the history of Physiology, especially as it developed in this country. I am interested in occasional consultive or advisory activities if they involve matters with which I have sufficient competence. Eileen and I are free to move to another area although at present we have no plans for doing so. We hope to do some travelling from time to time.

W. Doyne Collings to Horace:

Until your letter came, I had not thought about "joining" the august, distinguished senior group. But, inexorably, nature took care of that. On July 1, 1979 (after exactly 30 years at Michigan State) I will begin a one year leave of absence to be followed on July 1, 1980, with retirement as Associate Chairman Emeritus. Retirement plans are incomplete, but East Lansing will continue to be our residential base.

Jane Sands Johnson to Hal:

I do enjoy reading the letters from the retired physiologists but find it harder and harder to write of myself. I am still reasonably active at 85 years. I live in a very lovely home, near my beloved step-daughter. I enjoy music and walking is possible, though with a cane. At my age, I do considerable remembering. Among my cherished memories are my contacts with your family. My hobby is to browse in family geneology. Sands - my maiden name. It is interesting to learn what manner of people were my ancestors. They came to the colonies in 1626. A few were physicians, one such was a woman.

Falconer Smith to Hal:

I have enjoyed reading the letters from members whom I have known either personally or by reputation. It is hard to come upon a body of more active people to judge from the writings. They seem to peak into two categories. One group consists of those who remain active in their particular field of scientific interest, and a second group like myself, are enjoying their lives apart from the pursuit of science.

After leaving radiation biology laboratory at NCI, I went into the research grants operation of NI and retired from the Public Health Service in 1964. At the American University in Washington, DC, I enjoyed the stimulation of contact wit both students and a growing young faculty. I left the American University, Department of Biology in 1972 and we came to live in the beautiful and historic Shenandoah Valley near Harpers Ferry. I can't seem to keep from getting involved in Citizen's Associations or other civic activities. The latest is to help in the restoration of a community theater. It was built very early in this century and has recently been designated an historic landmark. We find that the whole rebuilding process seems nearly as complicated as a physiological research problem and evidently contains at least as many unknowns and unpredic ble factors as any good bit of biology.

We are enjoying life and fortunately have good health in our favor. Life is pleasant on our 23 acres and is made even sweeter with honey from our bee colony. We have a solar assist in heating our home and heat our enclosed swimming pool with solar units installed by - you guessed it! I have just learned how to join copper tubing, plastic tubing and pipe and have even dipped into the mysteries of electricity and wiring! We live only three miles from historic Harpers Ferry. Our place would make a good side trip for any who may be visiting Harpers Ferry, and I must add that every patriotic physiologist should make at least one trip to that restored town.

Hans Ussing to Hal:

I am gradually becoming aware of the fact that compulsory retirement is getting closer, although I have three years to go as a professor at the University of Copenhagen. So far it is business as usual, research, administration, teaching and writing books and scientific papers. On the research front I have been working on the theory of non-steady state flux ratios and other kinetic problems, and I am involved in a study of the volume regulation of epithelial cells and its relation to transepithelial ion transport. One highlight was giving the Dunham lectures at Harvard Medical School in the Fall of 1977. It was a great treat for my wife, Annemarie, and myself to meet old and new friends from the region. I do hope that I can keep contact with active research even after retirement, somewhere, somehow. If a suitable arrangement cannot be made here, I might be interested in some o her affiliation- for shorter or longer periods.

Physiology of Love

Consider, Lover, that the static little homunculus
tatooed on my brain
Feels all I feel in hand or tongue or face.
So, when we kiss, through circumferential routes
of fibers the dancing potentials race,
Letting our two homunculi synaptically embrace.

OBITUARY

The physiology and biophysics community was deprived of a friend, researcher and energetic teacher when Tushar K. Chowdhury, Professor of Physiology and Director of Biophysics Program at the University of Oklahoma, passed away on July 4, 1978 at age 41. After obtaining the Ph.D. in biophysics at State University of New York at Buffalo in 1965, his professional career was spent at that institution, at George Washington University and at the University of Oklahoma. A principal area of his work was transcellular transport. In the course of developing appropriate instrumentation, he devised certain scientific instruments that gained wide use. Other areas of Chowdhury's research interests included the cellular mode of action of antidiuretic hormone, electrochemical and conconavalin A effects on tumor cells, and cellular immunology. He was a member of several scientific societies. Dr. Chowdhury was also interested in the international aspects of science and participated or chaired in meetings in Jerusalem, Beirut, Cambridge, Vienna, New Delhi, and Moscow. He was thesis advisor to several doctoral candidates, carried a heavy administrative responsibility, and acted as adviser or reviewer for a number of journals and scientific organizations. Dr. Chowdhury became an author of four books and nearly 60 journal articles. He had compressed the activities of a much longer career into a 41 year lifespan. He is survived by his parents, wife and three children, by his scientist brothers and sister, and by his many students and colleagues. Those who knew him, or of his work, will miss his enthusiam, interest and devotion.

Eugene D. Jacobson, M.D.
Associate Dean
College of Medicine
University of Cincinnati Medical Center
Cincinnati, Ohio 45267

Richard P. Spencer, M.D., Ph.D.
Professor & Chairman
Department of Nuclear Medicine
Univ. Connecticut Health Center
Farmington, CT 06032

GENICHI KATO

Professor Genichi Kato, Keio University Medical School, Shinanomachi, Shinjukuku, Tokyo, Japan, died May 1, 1979.

Dr. John Brookhart, President of APS at the time, presented Dr. Kato with Honorary Membership in the Society during the XXIII IUPS Congress held in Tokyo in 1965. Letters of condolence may be written to Dr. Eiichi Kato, 9 Daikyocho Shinjukuku, Tokyo 160.

WILLIAM G. CLARK

APS Member, **Dr. William G. Clark,** internationally known researcher in psychopharmacology died February 13, 1979. He was 70 years old.

The Editor of *The Pharmacologist* plans to publish an obituary in Volume 21, Number 4, 1979.

Editor: Orr E. Reynolds, Education Office, APS
Associate Editors: Robert E. Fellows, Dept. of Physiology and Biophysics, University of Iowa
Mary Forsling, Middlesex Hospital Medical School, London, England
Ann E. Kammer, Division of Biology, Kansas State University
Charles S. Tidball, Dept. of Physiology, George Washington University Medical Center
Executive Editor: M. C. Shelesnyak, A.P.S.

THE PHYSIOLOGY TEACHER

NOVEL TECHNIQUES IN TEACHING PHYSIOLOGY

Discussion Meeting

Editor's Note:

Some months ago, Dr. Mary Forsling alerted my attention to plans for a meeting in London, on "Novel Techniques in Teaching Physiology." The material was all very suitable for consideration for publishing in *The Physiology Teacher.* Accordingly, we invited Dr. Forsling, who is an associate editor of *The Physiology Teacher,* to accept Guest Editorship for the proceedings of the meeting.

We are pleased to publish these papers and want to express our appreciation to British colleagues for their willing collaborations.

A meeting on novel techniques in teaching Physiology was held at Queen Elizabeth College (University of London) on the 16th of February, 1979. This turned out to be one of the coldest days of the year, snow and ice making travel difficult, if not impossible, in some instances. Nevertheless, the speakers, some from far afield, all appeared on time and some 85 participants braved the vagaries of the British climate to attend. The chair was taken by Professor J.H. Green, who has been tireless in his efforts to introduce new audio-visual techniques into the teaching of Physiology, both in the Middlesex Hospital Medical School and London University as a whole. The meeting was organized by the Audiovisual Aids and Computing Subcommittees of the Board of Studies in Physiology of London University under the auspices of the Subcommittee for Information and Education of the Physiological Society. Many physiologists in different schools have been developing new techniques for teaching physiology and it was felt that such a meeting would provide a forum where such material could be presented and ideas exchanged.

PROGRAMME

Meeting on Novel Techniques in Teaching Physiology

Time : 9.30-13.00 hours
Date : Friday, 16 February 1979
Venue : Queen Elizabeth College

9.30-10.00	Keynote Speech and Discussion	Professor C.J. Dickinson St. Bartholomew's Hospital Medical School, London

PAPERS AND DISCUSSIONS ON:

10.00-10.25	Tape slides/booklets in teaching Physiology	Dr. Mary Davies Chelsea College, London/ BLAT Centre, BMA House
10.25-10.50	Teaching Physiology by games and models	Dr. A.H. Short University Hospital and Medical College, Nottingham
10.50-11.15	A flexible student-oriented approach to Physiology practical teaching	Professor J.S. Lamb Bute Medical Buildings, St. Andrews University, Fife
11.15-11.45	COFFEE	
11.45-12.10	The use of television and videotapes	Professor W. Wiemer Universitatsklinikum der Gesamthochschule, Essen
12.10-12.35	The use of computer graphics	Dr. S. Lal Chelsea College, London
12.35-13.00	The role of computer models and computerised data bases in teaching Physiology	Dr. D. Ingram St. Bartholomew's Hospital Medical School, London

NEW IDEAS IN TEACHING PHYSIOLOGY

Dickinson, C.J.
Dept. of Medicine
St. Bartholomew's Hospital
West Smithfield, London, E.C.1.

There are several reasons for exploring new techniques in teaching physiology. Almost all current physiological research requires new techniques, and physiology teaching is not likely to be inspiring unless it has some relevance to present-day research. Although the textbook is likely to remain the cornerstone of physiological instruction, there are some interesting new developments and techniques for self-instruction which look promising. This symposium reviews some of them.

I shall start by briefly discussing perhaps the most sophisticated technique - the use of computer models. We should try to keep the number of animal experiments by students to a reasonable minimum. Leaving aside questions of cost, which

are important considerations these days, physiology teachers can only justify animal experiments where no alternative exists. Many experiments are conducted in physiology classes to teach integrative aspects of an organism, e.g. experiments on blood pressure stabilisation. Such classwork is often devised to teach the principles of integrative behaviour, rather than of cannulation of vessels or isolation of nerves. It seems more elegant, as well as more humane, to consider the use of simulation models for such work. Models also allow examination of dangerous and heroic experiments which might risk killing an animal, or severely damaging a human volunteer. Experiments with extreme hypoxia, for example, are interesting and have practical relevance to climbing mountains, to high altitude flying, and to clinical conditions in which lung function is poor. It is not really feasible to perform experiments of this sort either on animals or on man, but it can be stimulating and instructive to look at their consequences on a model.

Another advantage of a model, if it can run fast, resides in its speed *per se,* which enables several simulated experiments to be done in the time which would have been taken for one experiment.

Physical models have been used in physiology classes for more than forty years. Well known examples include simulation of the systemic circulation by fluid circulating in glass and rubber tubes and simulation of the processes of pulmonary ventilation by belljars and balloons. Computer models lack the robust and obvious realism of such physical models, but they are far more flexible and versatile, and far easier to use. In addition it is possible to combine the performance of a simulated experiment on a model with an associated explanatory text and questions, and to branch in and out of a model freely in accordance with the suggestions of the text dialogue. My colleague David Ingram describes in a later paper some examples of such a system.

A digital computer is not limited to output in digital or alphanumeric form. A digital type of output can plot certain primitive graphs, but graph plotters are becoming cheaper and more widely available, and it is in principle very simple to link the output of a model or computer-based class exercise in such a way that the model or program can be made to plot graphs which correspond to the user's instructions, or which reflect the results of a simulated experiment. Dr. Lal gives some examples of computer graphics display of physiological models in a later paper.

Most dynamic physiological models comprise a set of algebraic and differential equations, and numerous methods exist for solving these, and for displaying the results in some realistic way. My own stimulus to develop the first of the 'Mac' family of computer models was the challenge of teaching circulatory physiology to the first class of medical students at McMaster University Medical School, Canada, without the help of a practical classroom or animal laboratory. 'MacMan' (1) was designed to allow study of the basic systemic circulation including the solution of the simultaneous equations governing venous return and cardiac output, and of the way in which the arterial baroreceptor stabilising mechanisms respond to and correct disturbances of cardiac function and blood volume. The output was presented on a visual display unit, teletype or lineprinter in the form of vertical graphs of blood pressure and heart rate, with some key numerical values.

This model has been used with some success in many other medical schools, and my colleagues and I have developed various other more complex digital computer models, including 'MacPee' (combining the haemodynamics of MacMan with capillary exchanges, other body compartments and kidneys). 'MacPuf' (2) is so far the most compete and accurate model, and this describes pulmonary gas exchange and gas transport, with ventilation controls. It is capable of simulating a virtually infinite series of experiments on human subjects in health and disease. These models and several other, simulating the newborn infant in respect of gas exchange ('MacBabe'), diving and decompression ('MacDive') and pharmacokinetics ('MacDope') are at present available on magnetic tape, in standard Fortran IV, at a nominal handling charge (in most cases including the cost of handbooks) from Dr. D. Ingram in the Department of Medicine at St. Bartholomew's Hospital Medical College, London.

I do not claim that the models are perfect - far from it. However, any model is capable of being indefinitely improved, and my colleagues and I have already improved the models greatly with the help, advice and criticism of many who have used them. We hope that the process will continue.

REFERENCES

1. Dickinson, C.J., Sackett, D.I. & Goldsmith, C.H. (1973). MacMan: A digital computer model for teaching some basic principles of haemodynamics. *J. Clin. Computing* 2, 42-45.
2. Dickinson, C.J. (1977). *A computer model of human respiration.* Lancaster, MTP Press.

DISCUSSION

After Professor Dickinson's keynote speech:

J. Dickinson, V.R. Pickles (University of Cardiff), S. Lal, W. Wiemer.

In his opening speech, Professor Dickinson mentioned that only 30% students at MacMaster had taken up the option of using computer models of physiological systems. During the course of the discussion it transpired that this was due to a very full timetable which left the students with little extra time, so that they felt that any model systems had relatively low priority. When use of a model was integrated into a course and the instructor was totally familiar with the system, then it could be valuable and popular with the student. An example of this was the use of the model 'MacPee' in the intercalated B.Sc. Course on Renal Physiology organised by Dr. E.A. Ullmann at the Medical College of St. Bartholomew's Hospital. The models were at present being widely used - in some 100 Schools and Colleges throughout the world. There was some evidence that willingness to use computers depended on the background of the students; whether they had studied physical sciences.

Tape/Booklets in teaching physiology

Mary A. Davies, Department of Physiology, Chelsea College, University of London

Since Dr. Mary Davies had an article published so recently in *The Physiology Teacher,* she requested that an abstract only be published of her presentation together with a note to the effect that for further information the reader should refer to the earlier number of *The Physiology Teacher* (Vol. 21, No. 6, p.45, Dec. 1978).

Abstract

Self instructional material (SIM) in the form of audio cassettes and booklets is now being used in many departments of physiology. At least thirty units of self instructional material have been prepared by the Audio Visual Aids Sub Committee of the Board of Studies in Physiology (University of London) and the British Life Assurance Trust Centre for Health and Medical Education. The history of this project will be outlined and the

design of the material described and demonstrated. An evaluation carried out in two London Medical Schools indicated that the self instructional material is as effective as conventional methods of study in enabling students to achieve the stated learning objectives and is acceptable to students. The material is now being widely distributed in this country and abroad and its use and acceptablility by teachers and students evaluated by questionnaires. Preliminary results of this evaluation will be presented.

References

Introduction

Engel, C.E. (1970) Audiotape for self instruction. University Vision 5 *17-22*

Design

Engel, C.E. (1971) Preparation of audiotapes for self instruction. Medical and Biological Illustration 21 *(1) 14-18*

Evaluation

Davies, Mary A, Gale, Janet, Clarke, W.D. (1977) Audiotape and booklet selfinstructional materials in physiology: an evaluation of their effectiveness and acceptability in the pre-clinical curriculum. Medical Education 11 *370-373*

DISCUSSION:

After Dr. Mary Davies paper

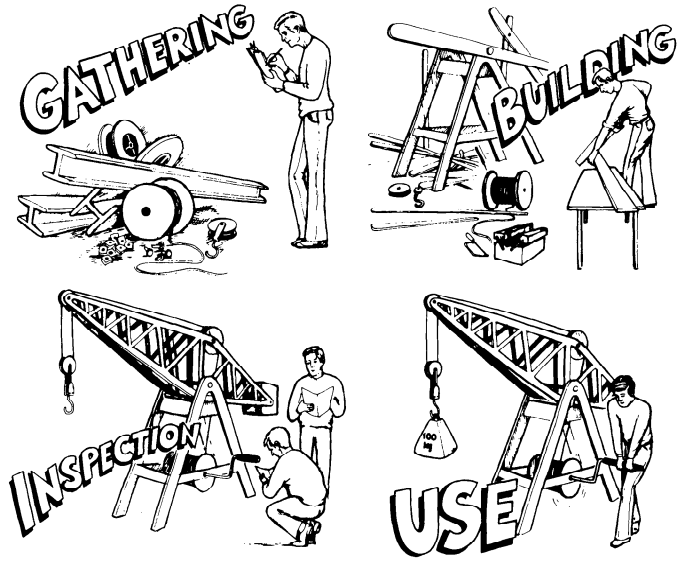
M. Davies, G.L. de Motta (University of Puerto Rico), S. Lal, L. Smaje (Charing Cross Hospital Medical School), W. Wiemer

In the discussion the question was raised as to how the groups of students who participated in the evaluation were chosen. Dr. Davies said that an entire class - 120 medical students from Charing Cross and 90 from St. Mary's Hospital Medical School participated in the evaluation and were randomly assigned into two groups, those using conventional teaching methods and those with audiotape/ booklets. Discussion then centred on the use of tapes within a course. The concensus was that such presentations could be used in place of lectures and for small group discussions. While the evidence showed that tape booklets were more effective than conventional methods, the question was raised as to whether this was due to the time and effort spent in the organisation of material for the tape/booklet presentation, rather than the medium itself. It was also pointed out that the attitude of the students to the medium may influence its effectiveness. In a study in New Zealand using audiotapes and texts, its was shown that both were equally effective, but the students learnt more quickly from the tape. While Dr. Davies had demonstrated the short term response after using tape booklets, Dr. Smaje presented the long term results on two successive years of students. The first group were given a lecture on a specific topic and the following year the second group were given on audiovisual presentation on the same topic. This second group performed better when tested at a later date.

TEACHING PHYSIOLOGY BY GAMES AND MODELS

A.H. Short
Department of Physiology and Pharmacology
University of Nottingham Medical School
Nottingham NG7 2UH.

The whole task of the medical student in the early years of the course can be described in terms of gathering materials, building conceptual models, testing and using them. This can itself be presented in terms of a model (Fig. 1), which indicates how modelling is a shorthand for concepts that are incompletely understood but useful in explanation. We can judge the quality of a student's grasp by seeing how well his models work. Some disappointing outcomes of learning are due to the learning sequence being arrested at too early a stage (Fig. 2).



We use many forms of modelling in explanation to our students, metaphor, diagrams, graphs, physical constructs, and games. The game and the physical construct are explicit forms of analogy which are less often used, so that although they are not novel methods in any general sense, they appear novel to the student and are valuable tools for this reason alone. It will, of course, be generally agreed that the best sources for the student's inner model-building will always be direct observation and experiment. Where these are not possible games and models offer alternative ways to complete the learning process.

Models

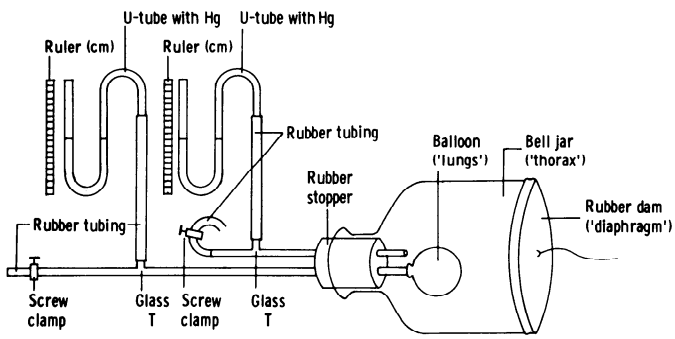
The term is here restricted to the use of physical constructs which in some attributes resemble the structures or processes which are the current objects of study. The plainest example is the anatomical model used to introduce, for example, the physiology of hearing by a greatly enlarged reconstruction of the organ of Corti.

Some simple mechanical models can assist the teacher to explain in the lecture room or laboratory class some of the less obvious physical facts of physiology. For example the behaviour of unequal soap-bubbles brought into communication with one another lends immediate conviction to a discussion of the Laplace relationship, or the behaviour of a fine suspended helical spring will demonstrate strikingly the inequality of stress on lung in the errect posture, and its change on recumbency.

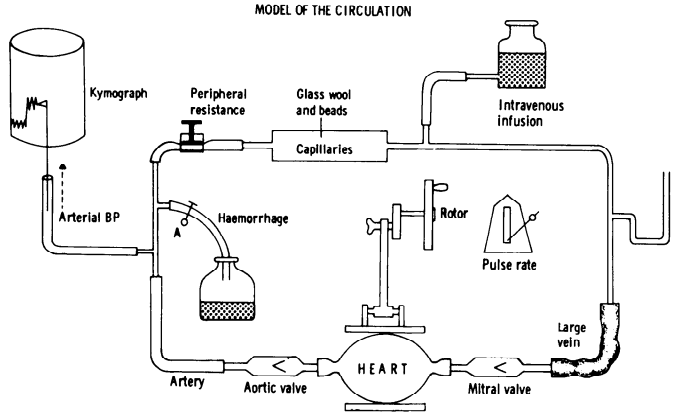
The interaction between the model and the student is greater where its physics parallel the modelled object, for example an optical model of the eye with which an opthalmoscope can be used. The power of a model with which the student can simulate for himself the effects of several variables may be even greater.

Examples of this are the lung-in-pleura-cavity model (Fig. 3) recommended by Tuttle & Schottelius (1968), and the mechanical model of the circulation (Fig. 4) invented by Professor Macdowall and described by Harris (1941). The student who had a leisurely opportunity to play with this model could hardly fail to grasp the main mechanical properties of the mammalian circulation, an accomplishment that unhappily evades many a student.

MODEL OF LUNG IN PLEURAL CAVITY



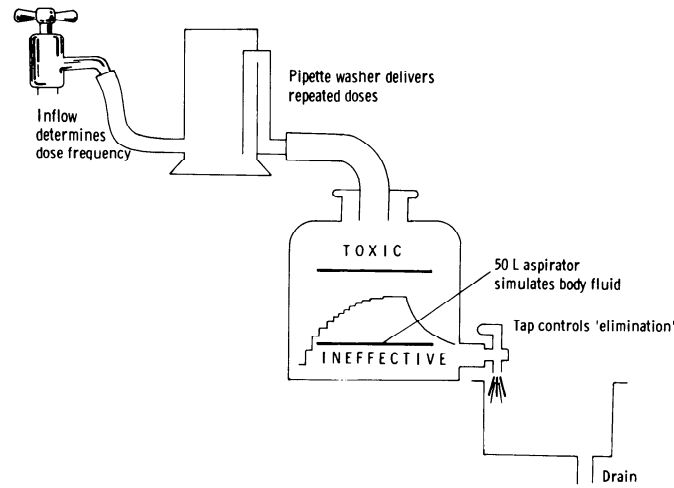
MODEL OF THE CIRCULATION



I have had considerable satisfaction from the success with which students have built for themselves models akin to that shown in Fig. 5, in order to explain principles of drug distribution in student-led seminar groups. An impressive suite of models is used by Dr. Roberts of Glasgow to demonstrate postural physiology. I will not attempt to deal with the use of analogue electrical circuits (used to illustrate propagated electrical disturbances, or the generation and management of acid-base distrubances) for these overlap some of the contributions on digital methods.

The benefits of use of models are the change of scale that is possible, the ability to bring out the significant properties of the system being studied and to suppress some of the distracting detail, to establish a common ground on which to build up an explanation, the opportunity the student may have to take the initiative and discover relationships by experiment, and freedom from the demands for experience, dexterity and resolution made by animal work. The caution which must be added is that a model can mislead if the student misconstrues the analogy on which it is based. It is necessary also to add that the pace of learning from the more complicated type of model must be allowed to be leisurely, and I suspect that things are so rushed in many cases that the results are disappointing and lead to the use of a model lapsing once the novelty to the teacher has worn off.

ELEMENTARY DRUG DISTRIBUTION



Games

Games differ from models in having a procedure, rules and a payoff. Teachers use these almost constantly both in teaching and assessment, but in an obscure fashion. Here we are concerned with games explicitly devised to promote some learning objective. The reasons why games deserve greater attention from teachers have been advanced elsewhere (Short, 1978). In brief, a good game engages sustained attention from learners, reinforces learning with each game cycle, entails learner initiative, requires appropriate use of information as well as mere recall, and should induce satisfaction with the subject matter rather than boredom or fatigue. The same reservations mentioned for models apply to games.

Suitable formats for academic games can always be found amongst existing pastimes. I take four widely known games as paradigms of these possibilities, namely 'I Spy', 'Rummy', 'Snakes and Ladders' and 'Cowboys and Indians'. The game of Respiratory Problem Solving, in which student groups take turns to compose the circumstances and observations appropriate to some respiratory emergency and by asking suitable questions to identify the problem, has been listed in the catalogue of Teaching Materials for Physiology from the 1977 Paris Congress. This corresponds to 'I Spy'. It is interesting that this simplest of game formats serves the highest level of cognitive objectives.

Many of the card games invented for physical science teaching, mostly in school-level chemistry and physics, prove to be variations on the theme of 'Rummy', that is, they cultivate the use of associations amongst the entities written on the card faces. A rather simple example intended for initial nurse training is 'Guts', in which the suits are foods, substrates, enzymes, reaction products and intestinal sites of absorption. A much more sophisticated one is 'CVS Rummy' devised by Dr. France at Kings College, in which the cards bear some 50 messages of which, for example "tachycardia, sympathetic stimulation, noradrenaline, haemorrhage" might constitute a group which the player laying down would have to justify to his colleagues. The very rich and

specific network of associations amongst such subject-matter promotes revision and reinforcement of cardiovascular physiology for all the participants. Another example covering a narrower area concerns drugs, antagonists and effects in the area of autonomic pharmacology has been named 'Pharmacanasta'. This game has been superceded by a board game ('Treat') mentioned below.

The 'Snakes and ladders' paradigm stands for all the board games regulated by dice in which the player encounters good and ill fortune as he covers the course towards an objective. I have not encountered a strictly physiological game in this category, but given that the choices are introduced as in Monopoly, it is a very powerful format for involving the player. I refer as educational examples to 'Citropoly', a biochemical game played to generate ATP (and inhibit the ATP production of opponents) and thus review cellular energy metabolism, and a recently devised elementary therapeutics game which may be called 'Treat', in which appropriate choice of treatments for the misfortunes that befall his "patients" as they made a circuit of the board enables the successful player to discharge all his patients from treatment.

'Cowboys and Indians' stands for all the simulation exercises in which players adopt roles within an agreed scenario and play out the roles inventively and more or less realistically. The example of this role-playing activity which uses physiological knowledge is the task of explaining to a simulated patient before a CCTV camera the nature of this newly diagnosed diabetes mellitus, or the significance of keeping to a diet to a simulated mother of a child with gluten enteropathy. A substantial part of the physiological knowledge needed by the future practitioner concerns his role in educating patients. A game helps to bridge the gap between learning and use.

SOURCES

CVS Rummy V.M. France, Faculty of Medical Science, King's College, London, WC2.

Citropoly M. Billett, Department of Biochemistry, University of Nottingham, NG7 2UH.

Guts Jean E. Lowe, NHS Learning Resources Unit, Sheffield City Polytechnic, Sheffield, S10 2NA.

Harris, D.T. (1941) 'Experimental Physiology for Medical Students' 3rd Edition, Churchill: London.

Pharmacanasta D.R. Tomlinson, Department of Physiology and Pharmacology, University of Nottingham, NG7 2UH.

Physiology of Posture Models T.D.M. Roberts, Institute of Physiology, Glasgow, G12 8QQ.

Respiratory Problem Solving A.H. Short, Department of Physiology and Pharmacology, University of Nottingham, NG7 2 U H .

Short, A.H. (1978) Learning by Game Medical Education, 12, 340-343.

Teaching Materials for Physiology Catalogue of materials exhibited at the Paris Congress 1977. The Physiological Society.

Tuttle, W.W., Schottelius, B.A. and Thomas, J.D. (1968) Physiology Laboratory Manual, C.V. Mosby St. Louis.

DISCUSSION

After Dr. A. Short's paper:
S. Lal, A.H. Short

The discussion centred on two main points namely the types of game available (role play, conflict and explorative) and the possible pitfalls associated with their use. There were few games available which allowed the student to explore the world. One game which might be considered as falling in this category was the Australian traffic accident game in which the students drew cards giving details of the nature of the injuries sustained, local conditions and the types of bystanders. The students had to decide what course of action to take and could compare their decisions with the information given on the backs of the cards. In using games there was always the danger that the students became so involved in the game that they failed to pay attention to the material to be learnt, although the possibility that students would sieze on the wrong feature of an analogy applied equally to the use of diagrams, models, games, etc. When games were used it was necessary to complete the session with a direct statement as to its aim or to have a debriefing or test session.

AUDIO-TUTORIALS: An effective alternative to traditional Physiology practical teaching?

by J.F. Lamb and N.L. Simmons
Department of Physiology and Pharmacology,
University of St. Andrews,
ST. ANDREWS,
Scotland.

Introduction

Traditional practical classes have always constituted a major portion of the time spent by students learning Physiology. The justification for this is that Physiology is an experimental science and so it is important for students to understand the experimental evidence and the underlying methodology (together with its limitations) upon which modern concepts are based. The traditional practical is a well-tried format and can be successful in achieving its objectives; this does not, however, exclude the possibility of the introduction of new methodology which may be more efficient. This paper describes our experiences with an audio-tutorial method of running our junior practical classes. The ideas upon which this system is based are not new, and in this we owe a considerable debt to the Department of Biochemistry of Dundee University (1) who run a similar audio-tutorial method of 'practical' teaching. The purpose of this article is not didactic but rather is to illustrate that alternative methods to traditional practicals can be successful, if only within the confines of our own situation.

This article is divided into 3 sections; firstly, the problems which lead to the adoption of a novel teaching method are considered, secondly, the solution to these problems are described (the audiotutorial) and finally, we ask whether the solution has been a success.

Problems

The Department of Physiology consists of 12 academic members of staff, three of whom are concerned solely with the teaching of Pharmacology. The Department offers and honours degree in Physiology, and teaches Physiology to pre-clinical medical students. The junior class in Physiology caters for approximately 175 student each year consisting of both science and pre-clinical medical students. Pre-1978 practical classes for this large group were run on a rota system with 9 separate experiments set out each week. Each student had one 2-hour laboratory session each week, and was expected to complete the 9 experiments in one term. Five separate laboratory sessions were timetabled each week to accommodate the large number of students. Both academic staff and postgraduate research students were involved in demonstrating during the 5 2-hour practicals. Costs were high due to the extensive use of postgraduate demonstrators. Student reaction to the practical

course was consistently disappointing. Dissatisfaction was expressed both at staff-student council meetings, and in response to a questionnaire. The reasons for this failure were numerous; the rota arrangement ensured that there was inadequate supervision, often of electro-physiological equipment (3 demonstrators were available for 35 students). Experiments were out of phase with lecture material so that the theoretical background was often lacking. Experiments frequently did not produce the 'correct' result, or old equipment simply failed. With the limitations of space provided by an old building, the inability of the department of re-equip with shrinking capital grants, and a decreasing population of postgraduate demonstrators, a reassessment of the way in which we taught our junior classes was inevitable.

Various choices were considered (experimental demonstrations, abolition of practical classes) and objections raised. Proven alternatives to the traditional practical are rare; such an alternative is that described by Macqueen, Chignall, Dutton & Garland (1) which itself is an adaption of an audio-tutorial method described by Postlethwait at Purdue University. We were impressed not only by the apparent similarity of the problems described by the Dundee department prior to change, but also at the obvious success of the system and its popularity with the students. A decision was therefore taken to change to the audio-tutorial system for our Junior class during the summer recess of 1978.

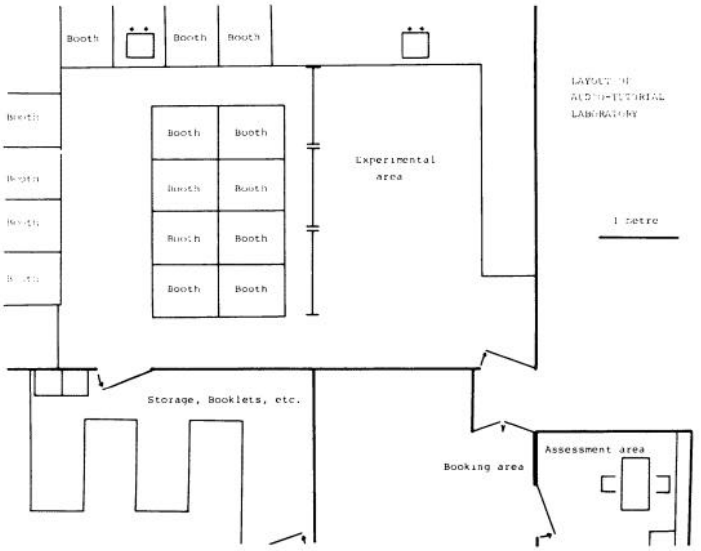
The Audio-Tutorial

(1) *Hardware.* The central feature of the audio-tutorial method is a tape-slide sequence. We chose a purpose-built sound-slide projector. The budget ($12,000) limited the number of such units to 16. The laboratory was modified with purpose-built easily movable partitions to form booths for the sound-slide projectors (Fig. 1). Also included in the laboratory were an experimental area, and assessment area and services. The space required is samall ($\sim 50 m^2$) and the laboratory is still easily modified for the traditional practicals run for other classes.

Slides were prepared in a departmental facility. Tapes and booklets were copied commercially. This extra cost amounted to approximately $200 per unit.

(2) *Operation.* In our system, each student 'books' a booth. On arrival he is given a booklet containing (i) the session objectives, (ii) a list of slides, (iii) some notes on the unit, and (iv) a list of self-assessment questions. At the booth containing the sound-slide projector, and a set of earphones, the student listens to the tape-slide sequence. Variety and movement during the sequence are provided by programming "breaks" for associated practicals, demonstrations and problem solving. On the following week the student attends an assessment session of 15 minutes duration at which he must pass seven out of ten question chosen at random from a bank of 100 questions. A failure to pass means that students must repeat the unit. Passes in all audio-tutorial units is a requirement for satisfactory completion of the course.

Table 1 shows the audio-turorial units for the junior class in Physiology. The main emphasis of the tape-slide sequences is the presentation of the experimental evidence underlying the various topics. Practical components to each unit do not pretend to be comprehensive. Simple practicals are performed whose success rate is high (approximately 95%); these practicals also demonstrate a part of the tape-slide sequence, i.e. in the sliding filament theory unit, students place various gratings in front of a laser to check the feasibility of measuring sarcomere length using first-order diffraction lines. In the control of growth hormone secretion unit, students perform an HCG pregnancy test as an example of a competitive protein binding assay. Problem solving



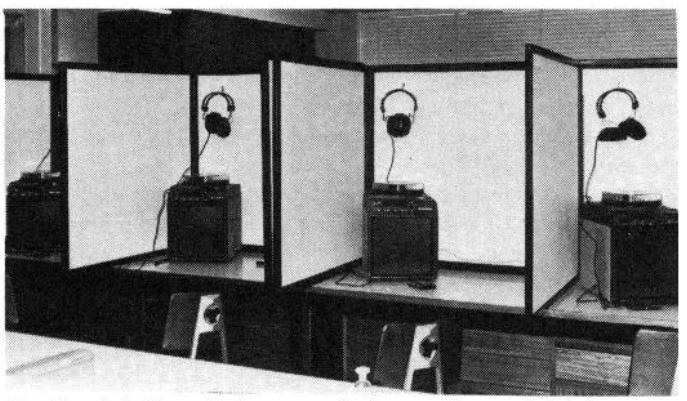


Fig. 1. (a) Overall lay-out of the audio-tutorial laboratory. Space is provided for booths containing the sound-slide projectors, an experimental area, services, and an assessment room.
(b) Booths are made from easily-moved partitions placed on benches.

emphasises numerical manipulation of experimental data, i.e. construction of length-tension diagrams, calculating sarcomere length from 1st order diffraction patterns, and the calculation of intracellular c-AMP levels from a c-AMP competitive protein binding assay. Posters and demonstrations emphasise clinical relevance (Ryles tubes in the gastric acid secretion unit) and can be made topical (e.g. a recent "Nature" article discussing the synthesis of growth hormone by mammalian genes inserted into bacteria).

The units are made to last 2 hours. Six 2-hour periods are run each week, and since we have only 16 machines, each audio-tutorial unit is run over a 2-week period. Students book into any 2-hour 'slot' within the two weeks, thus allowing great time-table flexibility. Thew assessments are run in a similar fashion, excepting that each last 15 minutes, and two members of staff officiate.

Assessments provide an unexpected bonus; good students come prepared to ask searching questions of the staff members; poor students find the one-for-one situation ideal for remedial instruction.

Staff involvement in this system is no greater than in traditional laboratories, though staff function has changed. Research orientated staff provide expertise in the preparation of the audio-tutorial units whilst teaching orientated staff provide the personal contact and continuity for the system. Postgraduate involvement is reduced; one demonstrator is able to service the entire practical laboratory since students complete various sections of the unit at

TABLE 1. Units in the junior class.

UNIT ONE The resting membrane potential.

Demonstration:	Microelectrode measurement of intracellular potentials.
Experiment:	Measurement of K^+ ion diffusion potentials across BDH-cation exchange membrane.
Problem solving:	Calculation of relative permeabilities of Na:K from biionic diffusion potentials.

UNIT TWO The sliding filament theory of muscular contraction.

Demonstrations:	Histochemical fibre typing of fast and slow twitch fibres. TS, LS electron-micrographs of skeletal muscle Laser diffraction patterns from gratings.
Problem solving:	Calculations of sarcomere lengths from 1st order lines of laser diffraction patterns. Length-tension diagrams.

UNIT THREE The control of gastric acid secretion.

Demonstrations:	Ryles-tube aspirations.
Experiment:	Titratable acid in basal and pentagastrin stimulated secretions.

UNIT FOUR Haematology (this unit departed from the usual format in describing the usual experimental manipulators, in red cell count, white cell count, haematocrit, etc.).

Experiment:	Total red cell count, white cell count, haematocrit, haemoglobin, differential white cell count.

ALL UNITS RUN AFTER THE APPROPRIATE LECTURES HAVE BEEN GIVEN.

different rates, and hence the number of students performing practical manipulations at any one time is reduced. This has the added benefit of reducing the amount of equipment required.

Success Of The System

The qualitative success of the audio-tutorial system may be judged by the lack of complaints received from students, indeed, they have been positively enthusiastic about the system. Whether this results from the novelty of the system is, as yet, unclear. In Dundee where a similar system has been operating for 4 years, this certainly is not the case. The system is popular with students for they (1) can learn at their own rate, (2) can repeat work as necessary, (3) have a flexible timetable, (4) find that the material on the tapes stretches them intellectually, and (5) find that assessment provides the necessary impetus for understanding difficult topics.

A questionnaire was devised, mainly to supervise the content, style, and clarity of the tape-slide sequences (2) The results of this survey indicate that students find the material in the sequences interesting. A proportion (26%) of students were keen to have the laboratory time extended to more than the 2 hours allotted. 97% of students also preferred the audio-tutorial system to traditional practicals as run by different science departments (mainly Anatomy and Biochemistry).

As in Dundee, the success of the system has encouraged us to extend this teaching method to other classes for certain of the usual practicals.

Summary

The application of an audio-tutorial method to teaching physiology practicals is described. The system is popular both with staff and students. The capital cost of such a system is modest, and the provision of semi-permanent material means that the system is cost-effective over a number of years.

REFERENCES

1. MacQueen, D., Chignall, D.A., Dutton, G.J., and Garland, P.B. (1976) Med. Educ., 10, 418.
2. Greive, I.B., Lamb, J.F., Neilson, J., and Simmons, N.L. (1979) Proc. of the Physiological Society, Queen Elizabeth Meeting J. Physiol. (in the press).

DISCUSSION

After Professor J. Lamb's paper:

G.E. de Motta, F.J. Imms (MRC Environmental Physiology Research Unit), J.F. Lamb, A.F. Rogers (University of Bristol)

Discussion concerned assessment of the practical and the way in which the laboratory was organised. The period of assessment also functioned as a tutorial. Students had to pass all units, but were not required to do so on the first attempt. The assessment was carried out by a demonstrator and certain members of staff. Members of staff running a course on a given topic were responsible for the assessment of the appropriate practical sessions. The laboratories were available for practical classes three days in the week, although the students could use the tape slide sequence at other times. Some students would attend several times to complete one unit. In conventional practical courses students often worked in pairs so that they could make measurements (e.g. blood pressure). In the system described there was still the opportunity for students to work together and there was considerable student interaction in the class. The students were not able to design their own experiments, but in providing this facility, one was catering only for a minority of students.

STUDIENMODELL PHYSIOLOGIE — A CONCEPT FOR THE INTEGRATION OF VIDEO—AND COMPUTER—TECHNOLOGIES INTO THE TEACHING OF PHYSIOLOGY IN THE FEDERAL REPUBLIC OF GERMANY (FRG)*

W. Wiemer and W. H. Anders
Institut fur Physiologie and Audiovisuelles Medienzentrum der Universitat Essen-Gesamthochschule, Hufelandstraβe 55, 4300 Essen 1 FRG

Physiology and the Situation of Medical Education in the Frg

In the FRG physiology is part of the preclinical medical curriculum extending over a minimum of four semesters. The present teaching problems in this field reflect the current situation of the 25 medical departments of the German universities: The total admission rate of medical students has soared up from about 4000 per year in 1968 to more than 11000 in 1978. The state government tries to cope with this rapid growth of student numbers by imposing on the traditional academic autonomy directives towards standardization and uniformity: The applicants - only about 20% of which are admitted every year - are not selected by the individual university, but by a central authority

*The Studienmodell Physiologie is supported by a grant from the Bund Länder-Kommission für Bildungsplanung und Forschungsförderung.

assigning the students to the universities on the basis of a complicated system integrating the grades of the school-leaving certificate (Abitur) and time factors since graduation. The quotas for the individual universities are set according to nationwide law, and based on the respective number of teaching personnel. Unfortunately, the increase of staff has by far not kept up with that of the student rate. Thus, the average student/staff ratio in physiology - as in other theoretical medical fields - exceeds at present 20:1 (!). The basic curriculum in medical education is also set by a federal law, the Approbationsordnung, and canonized in the so-called Gegenstandskatalog (1). During 2 or 3 semesters, the students are offered a series of lectures in physiology, usually on a non-obligatory basis; laboratory work, generally for the period of one semester, is compulsory. In accordance with the Approbationsordnung which recommends teaching in small groups, most departments offer additional seminars. Another controversial issue of the Approbationsordnung: the test for the laboratory work is the only examination still under the responsibility of the departments. All final examinations in theoretical and, partly, also clinical fields - in form of multiple choice questions - are carried out nationwide by a central board for medical examinations twice a year.

Current Role of the Use of Video-Technologies in Teaching Physiology in the FRG

During the last decade almost all departments of physiology in the FRG have been equipped with television facilities. The arguments for these considerable investments appeared convincing: The large audiences in the lecture halls required the demonstration of life experiments by television; the increasing difficulty to perform certain classroom experiments enforced the necessity to use audiovisual material. At least on the part of the political and financing authorities there was the hope to overcome the lack of personnel by providing funds for audiovisual equipment.

But apart from the (apparently rather modest) use for life demonstrations of classroom experiments video-technologies so far have failed to gain any degree of importance in teaching physiology in the FRG. Several interacting factors seem to be responsible for this failure:

The conceptual problem: The experimental phase of the use of modern technologies in education in the FRG - ranging from distant study models to large projects in CAI - has evidently not been able to dissipate the scepticism of many physiologists towards these novel techniques. The main arguments brought forth against the use of audiovisual material are that the selection of the subject-matter appears too specific to be readily transferable to other departments; the structure is regarded as too rigid to permit easy adaptation to other thematic or curricular contexts, or to even allow for the necessary replacement of obsolete parts. Apart from these arguments the general concept of educational technology and the individual learning approach is still being questioned, especially in relation to the effectiveness of the traditional forms of personal instruction. On the whole, the discussion on audiovisual and computer techniques - not only with a regard to self-instruction lessons, but also to such seemingly simple issues as video demonstrations in classroom - reflects the general lack of conclusive criteria for a systems approach and the conceptical framework for the use of video- and computer-technologies in higher education.

The production problem: With the exception of the "Vorlesungsbe-gleitendes Praktikum Neurophysiologie" (lecture-accompanying practical neurophysiology) by Henatsch, Göttingen (2) - originally produced for S 8 and audio-cassette presentation - there has been no large-scale systematic production of audiovisual or computer-based courseware for classroom or self-instruction purposes in physiology in the FRG. In related fields such as biology larger research and development projects have been funded, for example: Biologie fur Mediziner' (Hofmann, Cologne) framed on the learning centre concept by Postletwaith. A distant study concept for biology is being developed by the Faculty of Biology of the University of Tübingen. But these projects have not yet had any impact on the general situation. In addition, some physiology departments produced demonstration or instruction units of more or less experimental nature which, however, did not get known beyond the local scence.

One reason is that the facilities of the average physiology department with regard to both equipment and personnel proved insufficient not only for own production, but also for the adaptation of external material, particularly also from abroad. Evidently, video and computer courseware covering the essential range of the physiological subject matter could only be produced by cooperation of many departments. But such cooperations - for example, under the auspices of the German Physiological Society - have not yet been organized. Even then, the necessary level of media design as well as technical quality would require professionally equipped production facilities. At present, the only available institution of this kind in the FRG is the Institut Fur Wissenschaftlicher Film in Gottingen, which has only recently extended its activities from the classical research and documentation film to courseware including video-productions (3). The central advisory board for the developement of universities in the FRG, the Wissenschafts-rat, is preparing recommendations for the production of audiovisual material in medicine, proposing in every state a kind of regional production center affiliated with certain universities.

Thus, the presently available audiovisual material - which is collected and distributed by the Institut fur den Wissenschaft-lichen Film - consists mostly of films from various sources; it has remained fragmentary in the subject area covered, heterogenous in formate as well as concept and standard, and difficult to integrate into the curricular requirements.

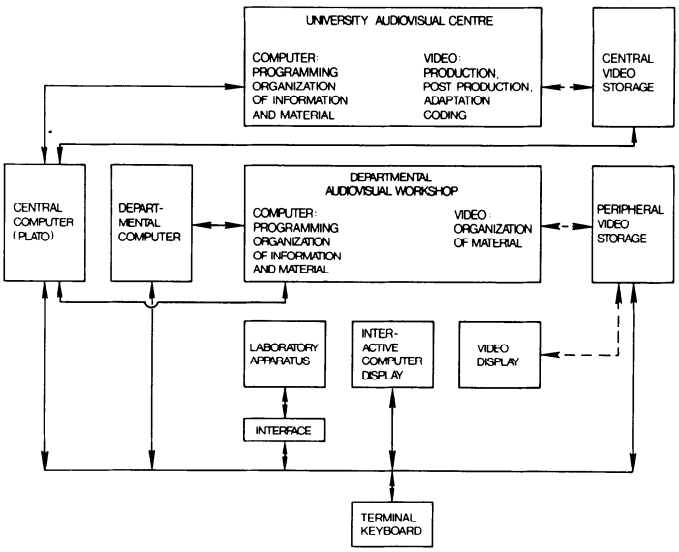
The technological problem: The video equipment and standards selected differ considerably from one institute to the other; these hardware concepts have hampered the exchange of teaching material considerably. Most departments are now equipped with color-TV, but few have the type of recorders providing the necessary picture quality. In addition, the present state of access to video-materials is mostly confined to manual operation of cassette recorders which is unsatisfactory for classroom and self-instruction terminals. Advanced systems providing automatic random access to materials and remote control to all display functions exist: In the FRG the PYRAMID-system approach has been further developed at Tübingen into a model for random access systems (4). But such systems are not generally available. Thus, the present technology still requires too much personnel, skill and time not only for production, but also for transfer, adaptation and presentation of video material. Consequently, many departments continue to present their audiovisual material on film and slides rather than on video basis, which severely limits the didactical context for the use of audiovisual materials.

The Studienmodell - an "Open" Concept on the Basis of Advanced Technology

In the past years, computer-based, interactive information and communication technologies have been developed (PLATO or TICCIT in the US), or are being developed (two-way-cable-TV)

which permit the use of video as part of a computer-controlled information system. A pilot-project "Studienmodell Physiologie" for teaching physiology based on this technology has now been started at the University of Essen in cooperation between the Department of Physiology and the Audiovisual Centre of the University. In consideration of the problems explained above, and similar experiences with video and computer-based teaching programs abroad the project does not only aim at technological improvement, but intends to develop a curricular system integrating audiovisual and computer instruction with classroom teaching, laboratory work, and self-instruction of students. The main aspects of this concept are:

Integrated technology: Technically, the model is based on the computer-controlled integration of video (as common carrier for film and slide material), computerized graphic and numeric instruction, and data analysis. This integration is achieved by a multi-functional audiovisual terminal consisting of a control keyboard, a dual display (VTR and computer) and an optional laboratory interface with A/D-converter for the direct measurement of experimental analogue data. The video material - marked by time code - is stored on computer-controlled tape recorder

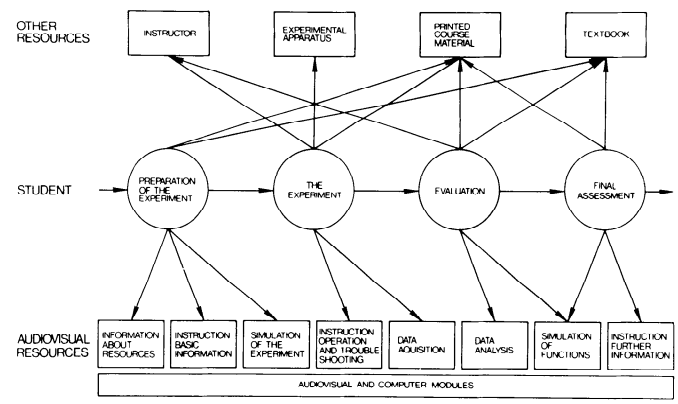


systems (BCN-Format) providing also still and slow motion replay. Two of these storage systems are used, one in the audiovisual center (for production, adaptation, and coding of the basic material), the other in the department of physiology (as central storage for the terminal positions). The system incorporates computer functions on two levels: the departmental computer (PDP-11, for minor control and instruction jobs) and the central computer furnishing the complete control and communication system (PLATO). Programming on the PLATO system can be done in the audiovisual centre as well as in the department. All peripheral functions can be controlled via the keyboard of the terminal (fig. 1).

Access and availability: Principally, all demonstration and instruction material will be available to the instructor as well as to the student. This is achieved not only by the computer-based handling of the material but also by a computerized information retrieval system containing curricular and thematic keywords about all units. This enables the student to organize self-instruction activities either according to thematic contexts of classroom teaching, or along his own lines of interest.

Modular structure: Physically, the integration of audiovisual and computer materials with teaching and self-instruction is achieved by the availability of terminals in lecture halls, seminars, laboratories as well as self-instruction places. The project does not aim at the development of coherent lessons; "open" mosaic like structures of small, thematically independant units are being prepared. With regard to computer-based instruction the emphasis will also not be on the informative type of lesson shaped on the traditional CAI approaches, but on interactive units with simulations of physiological and diagnostic functions. It is expected that such a modular structure will provide a practicable basis for flexible organization and reorganization of the audiovisual and CAI material within the department. The same material, or at least part of it, should then become usable in various didactic contexts such as class, seminar, laboratory and self-instruction, and also become adaptable to the local requirements of various departments. Since the production capacity of the audiovisual university center is, naturally limited, the pilot project will, as far as possible, make extensive use of already existing material (including foreign sources).

Fig. 2 illustrates the integration of personal instruction, printed instruction, laboratory apparatus and audiovisual and computer-assisted instruction in a student laboratory experiment: Along the course of this experiment, the student can call on various video or computer modules providing: general information about resources, basic information and simulation programs for this specific experiment, instructions for performing the experiment and acquiring the data, statistical evaluation of the data, and further instruction and simulation programs for final analysis.



Judged on the basis of one department and one project the financial background necessary to establish such a system approach is prohibitive. But surely it does not require prophetical gifts to state that computer-based information and communication networks will be generally available for educational purposes in the near future, making also university walls transcendable. Thus, the Studienmodell Physiologie seems to offer solutions for future use of such materials not only within the universities but also for extra-mural studies.

REFERENCES

1. Institut für medizinische und pharmazeutische Prüfungsfragen (Ed.): Gegenstandskatalog für die ärztliche Vorprufüng. Mainz 1976
2. Gerull, P., M.C. Tiffin und H.-D. Henatsch: Vorlesungsbegleitendes Praktikum Neurophysiologie - ein vorklinisches Ausbildungs-Modell. Med. Welt 28, 1229-1234; 1483-1488, 1977
3. Institut für den Wissenschaftlichen Film (Ed.): Filme in der Medizin. Göttingen 1977
4. Anders, W.H. und J. Wurster: Anwendungsmoglichkeiten der Breit-bandkmmunikation im Bildungswesen. Forschungsberichte des Bundes-ministeriums für Forschung und Technologie, Munchen 1977

DISCUSSION

After Professor W. Wiemer's paper:

S. Lal, W. Wiemer

The main issues dscussed concerned the advantages and disadvantages of centralised versus decentralised educational computing systems.

It was argued that the dedicated, large scale, main frame, educational computing system - such as the PLATO system - offered superior educational computing capabilities as well as significant financial cost advantages. Moreover, the relevant supporting software had already been fully developed and was readily available - an obvious consideration when local expertise was limited. The cost was, however, high.

Against this viewpoint, it was argued that a decentralised educational computing system which was organised around a collection of laboratory (or room based) microcomputing systems with interactive graphics capabilities offered not only financial benefits but also educational benefits as well. For cheap microcomputing systems with video output enabled data capture and anlysing, computing, interactive graphics, and library functions to be carried out on a single multifunctional system. Such computing set ups gave departments and institutions local control over educational computing and allowed for local initiatives based upon local requirements.

THE USE OF INTERACTIVE GRAPHICS

S. Lal

Dept. of Physiology, Chelsea College,
Manresa Road, London, SW3 6LX

INTRODUCTION

In this brief talk I shall attempt to sketch out answers to four main questions. Firstly, what topics and skills are best taught by means of interactive graphics? Secondly, what are the criteria which should be employed in choosing a graphics terminal? Thirdly, what are the educational 'costs' and 'benefits' of using interactive graphics? Fourthly, what are the most promising lines of development which need to be pursued if the full potential of interactive graphics in the tertiary educational context is to be fully realised?

In order to substantiate some of the claims I will make, I shall describe and demonstrate, at the end of this talk, two educational computing programs that employ interactive graphics. I shall also put forward a hypothesis about the use of interactive graphics in teaching basic scientific skills.

But first, I need to define what I mean by interactive graphics and by simulation. If (a) it is possible to display graphics (pictures, diagrams, graphs) and text with adequate resolution on a screen and (b) it is possible to change swiftly, simply and easily the displayed material, then an interactive graphics capability may be said to exist. Usually, this is provided by means of a terminal which may either possess its own microprocessor/microcomputer or is linked (by a comunication line) to a mini or mainframe computer. By simulation is meant the construction of a model (formed by equations representing a system or a situation) on a digital computer, so that something may be learned about the behaviour of a system or the changes in a situation. Users may experiment with the model by typing in various values of important parameters and variables and can receive printed or plotted displays of the results.

CHOICE OF TOPICS AND SKILLS

For the purpose of this talk, I shall duck some important educational questions and assume that the main educational aim of the teacher is to try and teach an 'average' group of undergraduate physiology students a variety of subject specific skills (ie. facts, concepts, laws and theories) and a variety of subject specific skills (experimental and theoretical). According to Lewis (1978), the following heuristic principle should be employed in selecting items to be taught by means of interactive graphics: choose those topics and skills which the student needs to be familiar with and which either the student finds difficult to grasp or which the teacher finds difficult to teach by conventional methods. Such a criterion, I think, enables the teacher to pick out five main areas of pedagogic difficulty. Firstly, many students cannot interpret mathematical statements (such as equations) or grasp their implications. They are, therefore, handicapped in dealing with analytically formulated relationships: their responses are either passive or aversive. Secondly, some students have problems in grasping the physical significance of theoretical and observational terms occurring in physiological theories which possess a certain mathematical content (eg. Hodgkin-Huxley theory or cable theory). Thirdly, a number of students have difficulty in interpreting and mainpulating experimental data, particularly when provided in a numerical form. Fourthly, students may have problems in grasping dynamic relationships between two or more linked variables. Finally, there are the student difficulties in getting an understanding of experimetnal techniques or designs which employ 'complex' (this usually means electronic) equipment.

A brief discussion of the use and value of interactive graphics in teaching such topics and skills may be found in Laurillard (1978) and Lal, Cunningham and Wood (1978). Briefly, interactive graphics enables analytically formulated or qualitatively specified relationships to be demonstrated in a controlled (rather than merely a stated) manner by the teacher. They allow the student the opportunity to 'experiment' with and explore such relationships and to get immediate feedback regarding their investigations in an intuitively intelligible form.

Among the more precise claims that may be made for interactive graphics are that: it increases motivation, it helps to develop critical thinking; it enables users to get a feel for the sizes and sensitivities of a system; it develops problem solving skills; it promotes hypotheses testing skills; it enables students to discover which variables are important in a situation; it permits the user to experiment with situations, not otherwise available - because the situations are too expensive or dangerous, or too time consuming to produce in a laboratory; it provides an opportunity to practice experimental and theoretical manipulations that a laboratory may not, or even cannot, provide. The rigorous testing of these claims remains a major field for educational research.

CHOICE OF GRAPHICS TERMINAL

A number of criteria such as plotting speed, resolution, graphics input capability, availability of hard copy, reproducibility of pictures on a videomonitor and cost have to be taken into account (Shirley, 1978). The consensus of opinion, such as there is, would seem to favour Raster scan displays with plotting speeds of at least 30 lines (vectors) a second, a resolution of at least 200 x 200 points, a graphics input capability of some kind, ability to repeat pictures on a videomonitor and a hard copier of some kind. The cost, excluding a hard copier and other peripheral devices, but including a microprocessor, should not exceed £1000.00 at 1977 prices (Shirley, 1978).

EDUCATIONAL 'COSTS' AND 'BENEFITS'

There is no universal agreement, except of totally vacuous kind as to what constitutes an educational cost or benefit. The most important benefit of interactive graphics, I hazard, has yet to be explicitly and fully exploited, viz. as a training ground for basic scientific skills and attitudes. Interactive graphics will enable the student to acquire a variety and range of research like investigatory experiences which it is impossible to provide by traditional means within the three years of a typical undergraduate physiology course. The main costs I suggest may be (1) an acceleration of the tendency to schematise and bureaucratise the curriculum; (2) a tendency to overemphasise the teaching of topics and skills that can be implemented by computer graphics; (3) the encouragement of a certain degree of laziness in formal theorising; (4) an undue reverence for what is taught via the interactive graphics route.

I have deliverately not pursued the issue of financial costs since not only are estimates of such costs a controversial matter, but the situation is a rapidly changing one. Some discussion of the financial costs and of the problems encountered in determining such costs may be found in Fielden (1978).

THE EDUCATIONAL FUTURE

The future lies, I think, in the use, of interactive graphics to create models of relationships, of processes, of systems, of environments, which the student can explore by experimentation, and thereby gain a practical effective knowledge of these 'worlds' and of the investigatory procedures (theoretical and experimental) which may be employed to investigate them.

I shall close by putting forward the following general interconnected set of testable hypotheses. Firstly, that many basic scientific skills can be identified, schematised and 'measured'. Secondly, that such skills can be explicitly and systematically taught. Thirdly, that proficiency in these skills can be significantly improved through the exposure of students to interactive graphics and computer assisted experimentation.

DESCRIPTIONS OF PROGRAMS DEMONSTRATED

Two interactive graphics programs were demonstrated using a Computer 300 raster scan graphics terminal linked by telephone to a DATA GENERAL NOVA 840. These were: BM8 AXON (VOLTAGE CLAMPING TECHNIQUE) and BM1 DYE3 (CARDIAC OUTPUT BY INDICATOR DILUTION).

The *AXON program* aims to teach the technique of voltage clamping as a method for identifying the ionic mechanisms involved in membrane phenomena - in particular the nerve action potential. It also enables the user to gain insight into the Hodgkin-Huxley theory particularly with reference to the initiation of the action potential. The pedagogic strategy involves the student performing a variety of voltage clamping experiments on a mathematical model of a squid axon. The student can get displayed in a graphical form the changes in (1) membrane current or (2) membrane conductance or (3) the m, n and h parameters resulting from the application of a voltage clamp. The clamping potential and the duration of the clamp are under student control. The user can change the sodium concentration in the external fluid and can add varying amounts of TEA and TTX. Displays can be obtained of the effects of changes in temperature and calcium concentration. In each case, the student can interrogate the graph by using a read cursor facility, and hence obtain the numerical values of the conductance or current or m, n and h parameters at any instant of time under the specified experimental conditions. From the data so obtained the student is able to estimate and analyse, for example, the ionic conductances as a function of time and membrane potential ie. the student measures the ionic current for a particular driving force and performs the relevant calculation.

The primary aim of *DYE3* is to teach the principles involved in the indicator dilution methods. The user selects the amount of dye to be injected into a vein and the program displays the dye concentration as a function of time. The program allows the student to alter various factors which go towards determining the shape of the concentration time curve. He can change: effective heart volume, injection rate, duration of injection, effective volume of circulation, distance between injection and sampling sites and cardiac output itself. The user can estimate the area under the graph (by means of a movable cursor) and hence the cardiac output.

The programs are currently being used in fifteen tertiary educational institutions in the U.K. and elsewhere.

ACKNOWLEDGEMENT

The two programs demonstrated form part of a suite of interactive graphics programs developed by the Computer in the Undergraduate Science Curriculum project. This project was supported by the National Development Programme in Computer Assisted Learning. Listings of paper tape of individual copies of programs and of the supporting documentation can be obtained for a price of £7.50 from the Educational Computing Section, Chelsea College, Pulton Place, London, SW6 5PR.

I wish to thank Dr. A. Wood and Mr. P.J. Murphy who collaborated in the development of the two programs demonstrated and Mr. R. Sellman for his help in mounting the demonstration.

REFERENCES

1. Fielden, J. Counting the cost: In Interactive Computer Graphics in Science Teaching. J. McKenzie, L. Elton and R. Lewis, Eds. Ellis Horwood: Chichester pp. 191-201, 1978
2. Lal, S., Cunningham, P. and Wood, A.W. CAL for Biology Ibid. pp. 132-147, 1978
3. Laurillard, Diana. Evolution and Evaluation Ibid. pp. 148-165, 1978
4. Lewis, R. and Murphy, P.J. Product design and development Ibid. pp. 20-30, 1978
5. Shirley, R. Graphical display for CAL Ibid. pp. 31-54, 1978

DISCUSSION

After Dr. Lal's paper:

S. Lal, J. Pascoe (University College, London), W. Wiemer

The relative merits of available computer graphics terminals and systems were debated. It was argued that current raster scan terminals, by virtue of their relatively poor resolving power and plotting accuracy, limited the educational employability of interactive graphics. Moreover, the need of a communicating link between a terminal and a computer could impose plotting speed restrictions which could significantly affect response times. It was agreed that the ideal system would be a vector refresh terminal, capable of colour displays, possessing its own microcomputer and backing store, usable as a free standing device. A larger, external, computer could then function either as a library or as a main frame device that could execute programs which exceeded the capabilities of the microcomputer based graphics terminal.

THE ROLE OF COMPUTER MODELS AND DATABASES IN THE TEACHING OF PHYSIOLOGY

D. Ingram
St. Bartholomew's Hospital
Medical School, London

Introduction

A great deal has been written on the subject of computer models, indeed they figure prominently in several of the other papers in this symposium. The range of biomedical research involving modelling and simulation has been reviewed by Groth (1) and the educational issues arising in the use of models in science teaching have been reviewed by Tawnay (2). Whereas ten years ago the role of modelling was largely a matter for speculation, the intervening years have seen a progressive broadening of applications in teaching and many teachers of physiology have gained practical experience of the problems and opportunities. It might well be said of statements today on the role of computerised data-bases, that they are speculative, As with modelling, the physical sciences have made a start first. Some areas of use of data-bases for assisting sharing and dissemination of fundamental data (for example, results of two body scattering experiments (3) are indications of the possibilities. I shall leave these speculations until my concluding section.

It would be rash to offer definitive statements regarding the role of modelling in teaching. I shall discuss what appear to be the main arguments for and against using models and then indicate some of the ways in which the computer models distributed from our department (4) and described by Professor Dickinson in his introductory paper, are being used.

Arguments for and against using computer models

The main general arguments which are advanced for using computer models are:

(i) To enable students to handle sometimes elaborate theoretical models flexibly and interactively. The emphasis is on using the computer to 'act out the theory' rather than as a replacement for experiment. This type of approach has proven more acceptable to students of a mathematical frame of mind or those who have had training in the physical sciences.
(ii) To allow rapid matching of model to experimental data, thus permitting the student to assess reasonable quickly how well the model explains the observed behaviour of the real system.
(iii) To avoid unnecessarily harmful experiments. This applies both to experiments using animal life or experiments on volunteer human subjects.
(iv) To simulate experiments where the technical skills may be beyond what can reasonably be achieved in a teaching laboratory.
(v) To speed up or slow down experiments in real life.

The main specific reasons put forward against the use of particular computer models are:

(i) That the models are inaccurate or inadequate representations of the real system.
(ii) That though accurate they are still unhelpful for teaching purposes.
(iii) That the interactive dialogue with the student and presentation of results is poorly designed and often repetitive and dull.
(iv) That the computers available for use in teaching are often unreliable and difficult to access.
(v) That computers are an expensive extra cost which cannot be afforded.
(vi) That the programs which have been written at one centre are difficult to transfer and incorporate in the curriculum of another centre.

The general points in favour of computer modelling are probably unexceptionable. More can be deduced about the role of modelling by looking at the objections in a little more detail since these give the measure of problems to be overcome in achieving a wider and more useful role.

Accuracy of models

The process of modelling involves creating, adapting and choosing among alternative representations and is inseparable from the process of testing. Like any scientific hypothesis, the model is always under suspicion. Inadequacy of computer models reflects inadequacy of theory, lack of quantitative data supporting theory or often difficulty in casting complex biological phenomena in tractable mathematical form. The process of modelling is one of simplifying the reality and representing it in its essential features. Application of such models to teaching has been called 'research coming down'. In physics there are instances where more than one model may be adopted to illustrate different freatures of the system under study. For example, the liquid drop and shell models of the atomic nucleus have been used to illustrate different aspects of stability of the nucleus. Absolute realism is an unachievable aim, but aspects of a system's behaviour may be well exemplified by simplified models.

Whether a computer model is adequate depends on the purpose for which it is intended and the criteria may differ according to the level of research or teaching considered. In most physiology teaching, the student uses an established theoretical model to simulate the behaviour of the real system and, for example, to explore how it reacts to various parameter changes. The exploration of alternative models and the construction of new models is a less common feature of physiology courses.

Usefulness in Teaching

There are two main sorts of reason why using a computer model may be unhelpful in teaching. On the one hand it may be because the model is too complicated and the program does not help students to sort out the essential features. On the other hand, too simple a computer model may merely illustrate the solution of an equation which is intuitively obvious to most students anyway. To be helpful, the value of insight achieved must in some way exceed the effort required in running the program. Even with the most sophisticated technology, it is unlikely to be helpful to use a computer model where a **simple** gragh makes the same point. With more complex models there is potential for useful teaching aids. For example, when learning about the oxy-haemoglobin dissociation curve for blood and the effects upon it of temperature, haemoglobin concentration, pH and pCO_2, the magnitudes of the shifts involved are not easily assimilated. Provided a model is simple to operate and preferably uses graphical output, it can be helpful.

Dullness of computer programs

This aspect of computer models is of no scientific importance but may, nonetheless, affect the reception of the model by students and the effort they will put into using it. A good deal of skill is required to avoid dull, repetitive interactive dialogue. Also the speed and form of output have to be carefully assessed. Once one is used to a certain standard of terminal, it is very difficult ever again to adjust to an inferior type.

ost and reliability of computer hardware

The economic aspects of computer-assisted learning have been carefully assessed by Fielden and colleagues as independent assessors of the U.K. National Development programme in computer-assisted learning (5). These matters are perhaps not readily decidable at present because of the rapid changes in price and performance of computers, the emergence of small dedicated microcomputer systems, and the increasing reliability of both hardware and software. The cost of preparation of good software is likely to rise and this makes it all the more important to achieve effective sharing. There is evidence of great duplication of effort on basic software. Standard systems will become widely transferrable and this will reduce the real costs of computer-assisted learning.

Communication of content of programs

Perhaps the most serious problem with many computer models is the lack of effective communication of their content. A thorough documentation of the model of human respiration, described by Professor Dickinson (6), covers some 300 pages of a monograph and is then not complete in every aspect. Yamamoto and Raub (7) have described how computer models of the regulation of breathing 'behave like indepndent, non-communicating physiologists'.

The only way to overcome such difficulties is by a wide dissemination of models and critical assessment and reporting back of faults by their users. The author also must take care to document all aspects of the program. Confidence in the validity of models and their relevance to teaching can only be achieved experimentally. We are now at a stage of wide scale experiment with computer models and the process will continue for many years with gradual emergence of useful and economically acceptable teaching aids.

A typical range of uses of 'MacPuf', a computer model of human respiration.

The model is usually implemented on a dedicated minicomputer or university timesharing service and is introduced to students with a lecture and demonstration. The main use has been as an extension of laboratory physiology practical work. Student experiments measuring, for example, oxygen uptake, blood gas tensions, cardiac output and ventilatory responses to CO_2 are simulated using the computer model and the students can then extend the results to other (perhaps more harmful) regions and observe the responses in the model. They are given free access to terminals during private study periods and typically about one-third of students find it profitable to investigate the model further in these periods, working through a set of problems provided in a user manual.

Finally the model is often used in tutorial classes and for revision purposes by students working alone. Similar applications have been reported to us across a wide range of undergraduate and postgraduate physiology teaching and with varying amounts of involvement. These range from use in practical classes only, to use in 'problem orientated' courses where the model is the central core around which the course is built.

In clinical teaching the use tends to be more specialised and related to particular relevant clincal techniques. Thus anaesthetists use the model for exploring various aspects of artificial ventilation and management of common respiratory disorders. This use has been found to be very helpful and popular, for example, with the professional training courses for anaesthetists at the Royal College of Surgeons in London over the past four years. It is always important to relate the results of simulation exercises to practical experience of clinicians dealing with patients.

One of the new developments which we have embarked upon has been the introduction of general tutorial exercises linked to the use of models. A file of text material is built up in a computer disc file (Fig. 1). This file is then interpreted by a driver program which is linked to the model. In this way a student may be led through a series of questions and his understanding assessed. Simulations may be generated directly by feeding a command string to the model from the disc file rather than from the student typing it on a terminal. Fig. 2 illustrates a section of a typical text file with commands to print text (frames starting with *T), ask questions (*Q) and run the model (*S). By combining eight different types of frame an extremely flexible dialogue can be arranged with free format input from the student. The student no longer has to master many of the details of how to run the model and simple interactive dialogue is possible. Fig. 3 illustrates a bag rebreathing experiment generated from a section of disc file. Another advantage of this approach is that the text material can be altered to meet the local requirements for presentation of the subject and the driver program includes an editor for this purpose. The system may be used for assessment purposes if required.

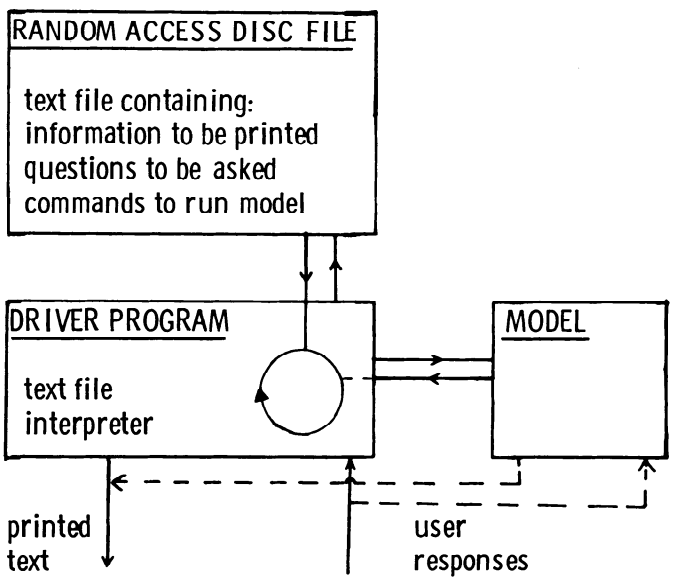


Fig. 1. The structure of an interpretive driver program linked to a computer model. This system allows very flexible and uncomplicated use of models for tutorials and assessment exercises.

```
 OK SO FAR?
*T 230 0 1 240 ************************************************************
 A FEW POINTS ABOUT THE MECHANICS OF DOING EXPERIMENTS
 ON 'MACPUF'.  WHEN YOU CALL UP MACPUF, YOU ARE GIVEN
 5 OPTIONS - 1(TO CHANGE THINGS), 2(TO CONTINUE),
 3(TO RESTART WITH A NEW SUBJECT), 4(TO INSPECT ALL THE
 VALUES) AND 5(TO STOP MACPUF AND COME BACK TO ME).
*Q 240 0 0 'CH',250 'GO',260 ************************************************
 IF YOU WANT TO CHECK ON THESE THINGS NOW, TYPE 'CHECK'.
 OTHERWISE TYPE  'GO',  AND I WILL SET YOU SOME CLINICAL PROBLEMS.
*S 250 0 3 260 ************************************************************
1/1/2
*Q 240 0 0 'RE',170 (1)270 (2)610 (3,5)760 ********************************
 HERE ARE SOME CLINICALLY RELEVANT PROBLEMS, WHICH I HAVE NUMBERED
 1 TO 5. THE GENERAL TOPICS COVERED ARE AS FOLLOWS:
 (1) CONCERNS ASPHYXIA (EG.BLOCKAGE OF THE TRACHEA)
 (2) CONCERNS THE LIMITATIONS TO EXERCISE PRODUCED BY HEART DISEASE
     AND LUNG DISEASE
 (3) CONCERNS THE EFFECTS OF CARDIAC ARREST
 (4) LOOKS AT THE CLINICAL PROBLEM OF VERY SEVERE ANAEMIA
 (5) IS CONCERNED WITH THE DIFFICULTIES OF CLIMBING
     MOUNT EVEREST.
 PLEASE NOW SELECT A PROBLEM, BY TYPING IN A NUMBER FROM
 1 TO 5.  OR YOU CAN TYPE 'RECAP' IF YOU IF YOU ARE NOT READY YET.
*F 270 0 1 280 ************************************************************
```

Fig. 2. A section of a text file prepared for a tutorial exercise in respiratory physiology. (See text for explanation of coding).

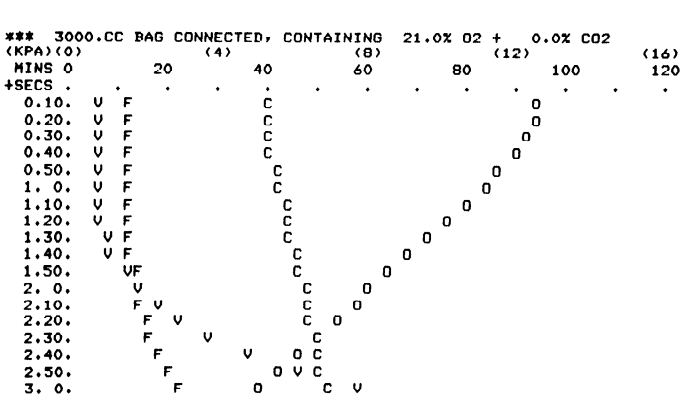


Fig. 3. Simulation of the effect of a subject rebreathing from a 3 litre air-filled bag. Symbols are V, total ventilation (1/min); F, frequency of breathing (min^{-1}); O, arterial pO_2 (mmHg or KPa); C, arterial PCO_2 (mmHg or KPa). The simulation is generated from a command coded in the text file and does not involve the student in typing commands to set up the simulated subject and alter model parameters.

Conclusion

The role of modelling may be expected to change with the rapid increase in power and flexibility of computer hardware. We have implemented our programs on several microprocessor systems and these are now at the point where a full working system can be purchased for about £4,000. In the near future we can expect systems to be available for this price which will support several users running the models. With current trends in the price of hardware, we can expect that within five years even the most complex of current biological models will run on systems which will cost in the region of £5,000 for a 32-bit processor with perhaps 128K words of memory. Thus the balance between cost and performance will continue to shift in favour of introduction of more sophisticated and comprehensive models of biological systems mounted in a form which will enable effective practical use by students. At present simplification is often forced on the modeller because of the need to ensure the short response times required for effective use in teaching. Cheaper processor power will help to remove such limitations and enable us to concentrate solely on the improvement of model quality and accuracy.

The possibility of maintaining large files of physiological data can be exploited in teaching in future. These data-bases are already in use in fundamental physics research to enable different theoretical groups to analyse common pools of high quality data which is difficult and costly to acquire. In biology there is already the reference data bank on atomic characteristics of body tissues (8) used in predicting effects of radiation therapy and the International Decompression data bank (9) which stores the results of diving experiments from many laboratories. We may expect data banks also to store material of interest in teaching, for example, the chemical characteristics of drugs, their interactions, and pharmacokinetic and pharmacodynamic properties.

REFERENCES

1. Groth, T., Biomedical Modelling Proceedings Medinfo 1977, Shires/Wolf Editors, IFIP/ North Holland Publishing Company, 1977, 775-784.
2. Tawnay, D.A., Simulation and Modelling in Science. Technical Report No. 11, Council for Educational Technology, London, 1976.
3. Gault, F.D., Information technology in particle physics Physics Bulletin 30, no. 2, 1979, 70-71.
4. Dickinson, C.J., Ingram, D. and Ahmed, K., The Mac Family of Physiological Models. ATLA Abstracts, 6, No. 2, 1978, 14-21.
5. Fielden, J., An approach to measuring the cost of computer-assisted learning. Technical Report No. 9, Council for Educational Technology, London, 1975.
6. Dickinson, C.J., A Computer Model of Human Respiration. M.T. Press Ltd., Lancaster, 1977.
7. Yanamoto, W.S. and Raub, W., Comp. Biomed. Res., 1, 196. 65-104.
8. ICRP Reference Man. Publication 23, International Commission on Radiological Protection, Pergamon Press, Oxford, 1975.
9. Lambertson, C.J. and Peterson, R.E., International Decompression Data Bank - Purposes, policies and procedures. Institute for Environmental Medicine, University of Pennsylvania, 1973.

DISCUSSION

After Dr. D. Ingram's paper:

D. Ingram, J.S. Lamb, W. Wiemer

It appeared that a major teaching problem to be overcome was the fact that students fail to see a system in an integrated way. Models used in a given course could help to rectify this. For example, in studying the cardiovascular system, a slide tape sequence combined with experiments and the use of MacMan could help the student greatly. Integration of material in this way could be achieved with the PLATO system.

BOOK REVIEW

Basic Clinical Physiology, J.H. Green. 3rd Ed., Oxford Univ. Press, New York, 1979. 176 pp. $9.95.

"Basic Clinical Physiology" condenses all of Physiology, some Pathophysiology and a smattering of Pharmacology into a compact text for beginners, particularly Allied Health students. The Cardiovascular System occupies one-third of the book, is well done and forms a good foundation for further study. Electrocardiography is introduced nicely and in a manner allowing further growth of the student's knowledge. The emphasis is upon a physiological explanation (whenever possible) for commonly observed medical events and occurrences - cardiac pacemaking for example. The slant is clinical.

The rest of the organ systems are done in a similar fashion, albeit in a more abbreviated form. It is easy to find fault with the many simplifications the author uses, such as "Na ions are prevented from entering the nerve cell by the sodium pump". I, for one, believe Dr. Green's simplifications are well chosen and of enormous use to the beginning Allied Health student. I do not believe "Basic Clinical Physiology" would be of value to American Medical students. The illustrations are well done and the index is extensive.

The British english presents a problem. Words are spelled or use differently, oedema = edema, torch = flashlight: syntax differs. Drug names present another more serious problem. Trade names vary on the two sides of the Atlantic, for example Lignocaine = Lidocaine. None of these problems should stand in the way of a bright, self-motivated student gaining much valuable information and insight from this book. Unfortunately the book's intended American audience needs much encouragement to read at all; I am afraid the English stylistic barriers this book adds are a dear price to pay for its contents. I would not hesitate to use the book for a Physician's Assistant or Nurse Practitioner class if it were "translated" into American; as it is, I would hesitate.

B.A. Curtis, Ph.D.
Department of Basic Sciences
Peoria School of Medicine

STUDIES ON THE RELEASE OF RENIN BY DIRECT AND REFLEX ACTIVATION OF RENAL SYMPATHETIC NERVES*

David E. Donald

Department of Physiology and Biophysics
Mayo Clinic and Foundation
Rochester, MN 55901

Although it has been clearly shown that an increase in renal sympathetic nerve activity results in an increase in the release of renin, there is considerable debate regarding the mechanisms through which this neural release of renin occurs, and of the role of the renal nerves in the regulation of renin release in normal and abnormal circumstances. This presentation will offer data concerning the release of renin during direct and indirect stimulation of the renal nerves, and will attempt to define, in part at least, some of the pathways involved.

A. *Direct Electrical Excitation of the Renal Sympathetic Nerves*

Stimulation of the decentralized renal nerves at frequencies of 10 to 20 Hz in anesthetized dogs and cats resulted in an increase in renin release (8, 42) that was accompanied by changes in renal hemodynamics and handling of electrolytes. In the dog, but apparently not in the cat, the increase in renin release was sustained throughout a 25 minute period of stimulation (15). Renal blood flow was reduced as a result of arteriolar vasoconstriction and there was a preferential shunting of blood away from the outer cortex (13). The urinary excretion of sodium and potassium was reduced, partly from the reduction in glomerular filtration rate and partly from the neurally induced increase in sodium uptake by the proximal tubules (1, 34). These findings suggest that activation of an intra-renal vascular mechanism (2), or a decrease in sodium load to the macula densa (23), or both are factors in the increase in renin release that results from high intensity stimulation of the renal sympathetic nerves. These changes in renal hemodynamics and electrolyte excretion did not occur when the stimulation frequency was less than 1 Hz but this low level excitation of the renal nerves still resulted in a sustained increase in renin release (18, 36). In this particular experimental situation it was concluded that the major mechanism for the increase in renin release was a direct action of the renal sympathetic nerves on the juxtaglomerular cells.

Stimulation at still lower frequencies (0.25 Hz) did not result in a demonstrable increase in renin release. However stimulation of the renal nerves at these low intensities during supra-renal aortic constriction, or the intravenous infusion of furosemide, augmented the increase in renin release due to these perturbations by some three and one-half times (40).

Thus excitation of the renal sympathetic nerves may activate one or all of the mechanisms (the intra-renal vascular receptor, the sodium load to the macula densa, and the direct sympathetic innervation of the juxtaglomerular cells) held principally to be responsible for an increase in the release of renin (10, 43). In addition, very low levels of renal nerve activity may facilitate the release of renin engendered by a stimulus which itself does not act through the renal nerves (11). These several pathways through which a change in sympathetic nerve activity may cause an increase in renin release can make it difficult to determine the particular mechanism responsible in a given situation.

B. *Indirect Excitation of the Renal Sympathetic Nerves*

I. *Electrical Stimulation of the Central Nervous System.* In anesthetized dogs and cats stimulation of electrodes implanted chronically or acutely at selected areas in the brain stem resulted in an increase in arterial blood pressure and heart rate, a decrease in renal blood flow and an increase in renin release (24, 28, 41). Acute or chronic denervation of the kidney abolished the increase in renin release. In the cat local alpha-adrenoceptor blockade of the kidney with phenoxybenzamine prevented the decrease in renal blood flow but not the increase in renin release that resulted from brain stem stimulation (28). Other studies have shown that the reduction in sodium excretion due to direct or reflex activation of the renal sympathetic nerves also is prevented by alpha-adrenoceptor blockade of the kidney (34, 45). Treatment with a beta-adrenoceptor blocking agent (propranolol 1 mg/kg i.v.) abolished the increase in renin release but not the decrease in renal blood flow that resulted from brain stem stimulation (28). In dogs intravenous administration of phenoxybenzamine (3-6 mg/kg) largely prevented the increase in arterial blood pressure that accompanied electrical stimulation of the medulla, but failed to suppress the increase in plasma renin activity (25). These observations would support the hypothesis that a direct action of the renal sympathetic nerves on the juxtaglomerular cells is the principal mechanism through which brain stem stimulation causes an increase in renin release in cats and dogs.

In non-anesthetized dogs stimulation of electrodes chronically implanted in the hypothalamus caused a 50% suppression of renin release. Stimulation was attended by a mean decrease in arterial blood pressure of 20 mm Hg and by an increase in heart rate and femoral arterial blood flow. Renal blood flow was unchanged. After renal denervation hypothalamic stimulation failed to suppress renin release. These data from conscious dogs suggest there is a resting tonic sympathetic discharge to the juxtaglomerular cells which can be inhibited by localized hypothalamic stimulation (47).

The several studies show that excitation of discrete areas within the brain stem and hypothalamus can increase and decrease the release of renin through appropriate changes in activity of the renal sympathetic nerves, possibly by a direct action of the nerves on the juxtaglomerular cells.

II. *Role of Carotid and Cardiopulmonary Receptors.* Carotid sinus hypotension results in a generalized increase in sympathetic adrenergic activity that includes the renal nerves. This is attended by an increase in renal vascular resistance, a change in the intra-renal distribution of blood flow and a decrease in the urinary excretion of sodium mainly due to an increased uptake of this ion in the proximal tubules (45). It was therefore surprising to find marked divergence of opinion regarding the contribution of the carotid baroreflex to the neural control of renin release. Of twelve published studies, six affirm (7, 9, 12, 14, 22, 27) and six deny (4, 5, 16, 29, 32, 33) a significant role to the carotid baroreceptors in the reflex control of renin release. For example, Brennan and colleagues failed to find any significant correlation between changes in carotid sinus pressure and

*Tutorial Lecture, Fall Meeting 1978. American Physiological Society

Based on work supported by US Public Health Service Grant HLO 6143 from the National Institutes of Health

changes in plasma renin activity and concluded that the carotid baroreceptors played no significant part in the reflex control of renin release (4). In direct contrast Cunningham and colleagues recently demonstrated a rapid and sustained elevation in plasma renin activity during forty minutes of bilateral carotid occlusion (9). In the two studies in cats reported to date bilateral carotid occlusion did not result in any significant increase in plasma renin activity (5, 16).

A possible explanation for these widely differing observations will be discussed later.

In contrast to the dubiety regarding the role of the carotid baroreceptors there is nearly complete agreement concerning the part played by vagally innervated cardiopulmonary receptors in the reflex control of renin release.

Hodge and colleagues reported in 1969 that cervical vagal cooling or section caused an increase in circulating angiotensin in 9 of 12 dogs studied and suggested that afferent fibers in the vagus nerves could modulate the activity of the renal sympathetic nerves and thereby influence the release of renin (12). Support for this hypothesis came from the demonstration that dogs with chronic cardiac denervation had a subnormal increase in plasma renin activity in response to hemorrhage (37), and that increases (3) and decreases (6) in right atrial pressure not accompanied by other hemodynamic effects resulted in respective decreases and increases in renin release. Still further evidence was offered by the systematic studies of Mancia in 1975 (20) and Zehr in 1976 (46). The former study used dogs with aortic nerves sectioned and the carotid sinuses either denervated or vascularly isolated and maintained at a constant pressure of 140 mm Hg or less. Vagal block in these animals resulted in a substantial reversible increase in renin release that was prevented by prior denervation of the kidney. The increase in renin release was accompanied by moderate increases in arterial blood pressure (+12%) and decreases in renal blood flow (−8%). The increase in renin release did not appear correlated with the magnitude of the hemodynamic changes. A later independent study confirmed these findings (44).

That increased activity of left atrial receptors with vagal afferent nerves could suppress the release of renin was demonstrated by Zehr and colleagues in dogs that had been maintained on a low sodium diet prior to study (46). Increase in left atrial pressure (+5 cms H_20) by balloon obstruction of the mitral valve depressed renin secretion to 56% of its control value. Balloon inflation caused a slight increase in heart rate (+10%) but no changes in arterial and central venous pressure or in renal blood flow. The suppression of renin release on left atrial distention was prevented by prior cervical vagotomy or renal denervation.

Increased activity of vagally innervated ventricular receptors also was shown to suppress the release of renin in anesthetized dogs (38). An injection of cryptenamine, a veratrum alkaloid, into the left coronary artery was used to activate left ventricular receptors in dogs in which renin release had been increased by a 10 ml/kg hemorrhage. Renin release fell from a mean value of 1971 ng/min to 269 ng/min 4 min after the cryptenamine injection. The suppression of renin release was accompanied by a fall in arterial pressure but no change in renal blood flow. Vagotomy abolished this reflex suppression of renin release by excitation of ventricular receptors.

An increase in renin release has been reported to follow cervical vagotomy in the cat. In one of the studies the aortic nerves remained intact after cervical vagotomy (35) in the other the aortic nerves were cut at the time of vagal nerve section (5). Volume expansion with saline prevented the renin-releasing action of vagotomy in one study (35) but allowed it in the other (5).

Although the studies differ in certain details it would seem established that increase and decrease in activity of vagally innervated cardiopulmonary receptors can, by acting through the renal sympathetic nerves, respectively decrease and increase the release of renin. There is however one dissenting voice. Schrier and colleagues have described a decrease in renin secretion to follow bilateral cervical vagotomy in dogs undergoing a water diuresis. Vagal section in acutely hypophysectomized dogs failed to alter renin secretion. The authors suggest that ablation of vagal tone stimulated the release of vasopressin which in turn suppressed renin secretion, possibly by a direct effect on the juxtaglomerular cells (31). It should be noted that in these studies the aortic nerves were cut concurrently with the section of the vagal nerves. No explanation for this different response to vagotomy can be offered at this time.

To return to the question of the neural control of renin release by the carotid sinus baroreceptors; several studies have demonstrated an interaction between the carotid and the cardiopulmonary baroreceptors in the reflex control of the circulation (17, 19, 21). Recently it has been shown that these two systems also interact in the neural control of renin release. In 17 of 20 anesthetized mechanically ventilated dogs with aortic nerves cut but carotid sinuses intact, vagal cold block caused an increase in arterial blood pressure but not in renin release (39). It was thought that the increase in arterial pressure following vagal block might increase the inhibitory traffic from the carotid baroreceptors sufficiently to prevent an increase in renal sympathetic nerve traffic and thus suppress the reflex release of renin. Support for this hypothesis came from the demonstration of an increase in carotid sinus nerve activity during vagal cold block, and of an increase in renin release only when buffering activity of the carotid baroreceptors was prevented by their vascular isolation. Conversely reduction of carotid sinus pressure to 40 mm Hg in dogs with renal arterial pressure maintained constant failed to cause an increase in renin release in 7 of 10 dogs with intact vagal nerves. After cervical vagotomy carotid sinus hypotension increased the release of renin in 9 of the 10 dogs (14).

Thus although withdrawal of the inhibitory activity of each system separately can excite increase in renin release, if reduction in activity of one system results in concomitant activation of the other, than the expected increase in renin release may not occur. These studies also revealed a further restriction on the release of renin during carotid sinus hypotension (14). If renal arterial pressure were allowed to rise equally with systemic arterial pressure no increase in renin release occurred.

If the previous studies in the literature are examined in the light of these findings, the previous divergent observations on the effects of carotid sinus hypotension can be explained. Only in those studies in which the animals were vagotomized and in which renal perfusion was held constant did carotid sinus hypotension result in consistent and significant increases in renin release (7, 9, 14, 22, 27).

The observation that withdrawal of inhibitory nerve traffic from carotid sinus baroreceptors resulted in an increase in renin release only when there had been prior interruption of aortic and cardiopulmonary baroreceptor inhibition, and that withdrawal of inhibitory traffic from cardiopulmonary baroreceptors likewise only resulted in an increased release of renin if the carotid and aortic baroreceptors first had been denervated or prevented from exerting their buffering capacity raised the question that interference with all three receptor systems was necessary to promote an increased release of renin. The following experiment indicated this was not the case (39). In 10 dogs with aortic nerves cut but carotid sinuses intact a nonhypotensive hemorrhage (4

ml/kg) caused an increase in renin release. A similar hemorrhage after vagotomy failed to cause an increase in renin release in 7 of the 10 animals. Nine of 11 dogs bled before and after vagotomy had an increase in renin release on both occasions. During the second hemorrhage 70% of the vagotomized dogs did not have an increase in renin secretion compared to 18% in the sham-operated group. This difference is significant. Hemorrhage of this modest amount causes a fall in right atrial pressure but not in arterial blood pressure, and there was no reduction in carotid sinus nerve activity. The experiments allow the following conclusions. An increase in renin release will occur on reduction in inhibitory activity of one of the three peripheral receptor systems if such withdrawal does not change the activity of the other two. Vagally innervated cardiopulmonary receptors exert a tonic inhibition of renin release. Cardiopulmonary receptors are more sensitive to modest decreases in blood volume than are the carotid baroreceptors.

Finally the vexed question of the role of alpha and beta adrenoceptors in the release of renin resulting from increased activity of the renal sympathetic nerves. It is generally agreed that beta blockade alone or in combination with alpha blockade will prevent a neurally-engendered release of renin (10). There is considerable disagreement however regarding the effects on renin release of alpha-adrenoceptor blockade per se. In the cat direct stimulation of the renal nerves causes an increase in plasma renin activity that is prevented by prior treatment with the alpha-adrenoceptor antagonist phentolamine (8). In the same animal the increase in renin release resulting from stimulation of the brain stem is still obtained after local alpha adrenoceptor blockade of the kidney with phenoxybenzamine (28). The same agent administered intravenously to dogs in a dose of 3 to 6 mg/kg failed to suppress the increase in plasma renin activity produced by electrical stimulation of the medulla oblongata (25). In our laboratory local alpha adrenoceptor blockade of the kidney reduced the basal level of renin release and abolished the increased release due to carotid sinus hypotension. Local alpha adrenoceptor blockade with phenoxybenzamine also suppressed the increase in renin release resulting from electrical stimulation of the decentralized renal sympathetic nerves (26). These totally opposed findings emphasize the comment in a recent review that "the controversy regarding the effect of alpha-adrenoceptor blockade on renin release remains to be resolved" (30).

This limited survey of the neural control of renin release raises more questions than it answers. One point however seems clear. In controlled experiments change in the activity of the carotid and of the cardiopulmonary baroreceptor systems can influence the release of renin. This response however may be blunted or suppressed in a more intact preparation where the receptor systems are free to interact with each other, or when there are concomitant changes in renal hemodynamics and in the handling of electrolytes.

The author wishes to acknowledge the contributions of Drs. J. T. Shepherd, J. C. Romero, G. Mancia, P. N. Thorén, M. Jarecki, D. M. Powis and M. D. Thames to the studies which form the basis of this presentation, the technical expertise of Messrs. L. Aarhus and B. Howard, and the secretarial assistance of Ms. Jan Applequist.

REFERENCES

1. Bello-Reuss E., D. L. Travino and C. W. Gottschalk. Effect of renal nerve stimulation on proximal water and sodium reabsorption. *J. Clin. Invest.* 57:1104-1107, 1976.
2. Blaine, E. H. J. O. Davis, and R. L. Prewitt. Evidence for a renal vascular receptor in control of renin secretion. *Am. J. Physiol.* 220:1593-1597, 1971.
3. Brennan L. A., R. L. Malvin, K. E. Jochim and D. E. Roberts. Influence of right and left atrial receptors on plasma concentrations of ADH and renin. *Am. J. Physiol.* 221:273-278, 1971.
4. Brennan L. A., A. L. Henninger, K. E. Jochim and R. L. Malvin. Relationship between carotid sinus pressure and plasma renin level. *Am. J. Physiol.* 227:295-299, 1974.
5. Brosnihan K. B. and R. M. Travis. Influence of the vagus and the carotid sinus nerves on plasma renin in the cat. *J. Endocr.* 71:59-65, 1976.
6. Brosnihan K. B. and E. L. Bravo. Graded reductions of atrial pressure and renin release. *Am. J. Physiol.* Heart Circ. Physiol. 4: H175-H181, 1978.
7. Bunag R. D., I. H. Page and J. W. McCubbin. Neural stimulation of release of renin. *Circ. Res.* 19:851-858, 1966.
8. Coote, J. H., E. J. Johns, V. H. Macleod and B. Singer. Effect of renal nerve stimulation, renal blood flow and adrenergic blockade on plasma renin activity in the cat. *J. Physiol. (Lond)* 226:15-36, 1972.
9. Cunningham S. G., E. O. Feigl and A. M. Scher. Carotid sinus reflex influence on plasma renin activity. *Am. J. Physiol.* Heart Circ. Physiol. 3: H670-H678, 1978.
10. Davis J. O. and R. H. Freeman. Mechanisms regulating renin release. *Physiol. Rev.* 56:1-56, 1976.
11. DiBona G. F. and M. D. Thames. Role of renal nerves in renin release. *Clin. Res.* 26:541A, 1978.
12. Hodge R. L., R. D. Lowe and J. R. Vane. Increased angiotensin formation in response to carotid occlusion in the dog. *Nature* 211:491-493, 1966.
13. Houck C. R. Alterations in renal hemodynamics and function in separate kidneys during stimulation of renal artery nerves in dogs. *Am. J. Physiol.* 167:523-530, 1951.
14. Jarecki M, P. N. Thorén and D. E. Donald. Release of renin by the carotid baroreflex in anesthetized dogs. Role of cardiopulmonary vagal afferents and renal arterial pressure. *Circ. Res.* 42:614-619, 1978.
15. Johnson, J. A., J. O. Davis and R. T. Whitty. Effects of catecholamines and renal nerve stimulation on renin release in the nonfiltering kidney. *Circ. Res.* 29:646-653, 1971.
16. Kirchner V. F., F. Lamprecht, A. Phillip and R. Steinriede. Die Beziehung Zwischen der Aktivitat Sympathischer Nierennerven und der Plasmareninaktivitat bei narkotisierten Katzen Zeitschrift fur Kreilaufforschung 61:52-59, 1972.
17. Koike H., A. L. Mark, D. D. Heistad and P. G. Schmid. Influence of cardiopulmonary vagal afferent activity in carotid chemoreceptor and baroreceptor reflexes in the dog. *Circ. Res.* 37:422-429, 1975.
18. LaGrange R. C., C. H. Sloop and H. E. Schmid. Selective stimulation of renal nerves in the anesthetized dog. Effect on renin release during controlled changes in renal hemodynamics. *Circ. Res.* 33:704-712, 1973.
19. Little R., G. Wennergren and B. Oberg. Aspects of the central integration of arterial baroreceptor and cardiac ventricular receptor reflexes in the cat. *Acta Physiol. Scand.* 93:85-96, 1975.
20. Mancia G., J. C. Romero, J. T. Shepherd. Continuous inhibition of renin release in dogs by vagally innervated receptors in the cardiopulmonary region. *Circ. Res.* 36:529-535, 1975.
21. Mancia G., J. T. Shepherd and D. E. Donald. Role of cardiac pulmonary and carotid mechanoreceptors in the control of hindlimb and renal circulation in dogs. *Circ. Res.* 37:200-208, 1975.
22. McPhee M. S. and W. H. Lakey. Neurologic release of renin in mongrel dogs. *Can. J. Surgery* 14:142-146, 1971.
23. Nash F. D., H. H. Rostorfer, M. D. Bailie, R. L. Wathen and E. G. Schneider. Renin Release. Relation to renal sodium load and dissociation from hemodynamic changes. *Circ. Res.* 22:473-487, 1968.
24. Passo S. S., T. A. Assaykeen, K. Otsuka, B. L. Wise, A. Goldfin and W. F. Ganong. Effect of stimulation of the medulla oblongata on renin secretion in dogs. *Neuroendocrin.* 7:1-10, 1971.

25. Passo, S. S., T. A. Assaykeen, A. Goldfien and W. F. Ganong. Effect of α- and β-adrenergic blocking agents on the increase in renin secretion produced by stimulation of the medulla oblongata in dogs. *Neuroendocrin.* 7:97-104, 1971.
26. Powis D. A. and D. E. Donald. Involvement of renal α- and β-adrenoceptors in the release of renin by the carotid baroreflex. Accepted for publication. *Am. J. Physiol.*, 1979.
27. Reid I. A. and A. Jones. Effects of carotid occlusion and clonidine on renin secretion in anesthetized dogs. *Clin. Sci. Mol. Med.* 51:1095-1115, 1976.
28. Richardson, D., A. Stella, G. Leonetti, A. Bartorelli and A. Zanchetti. Mechanisms of renal release of renin by electrical stimulation of the brainstem in the cat. *Circ. Res.* 34:425-434, 1974.
29. Rocchini A. P., J. R. Cant and A. C. Barger. Carotid sinus reflex in dogs with low to high sodium intake. *Am. J. Physiol.* Heart Circ. Physiol. 2:H196-H202, 1977
30. Schrier R. W. Effects of adrenergic nervous system and catecholamines on systemic and renal hemodynamics, sodium and water excretion and renin secretion. *Kidney International* 6:291-306, 1974.
31. Schrier R. W., I. A. Reid, T. Berl and L. E. Early. Parasympathetic pathways, renin secretion and vasopressin release. *Clin. Sci. Mol. Med.* 48:83-89, 1975.
32. Schmid H. E. Renal autoregulation and renin release during changes in renal perfusion pressure. *Am. J. Physiol.* 222:1132-1137, 1972.
33. Skinner S. L., J. W. McCubbin and I. H. Page. Control of renin secretion. *Circ. Res.* 15:64-76, 1964.
34. Slick G. L., A. J. Aguilera, E. J. Zambraski, G. F. DiBona and G. J. Kalayanides. Renal neuroadrenergic transmission. *Am. J. Physiol.* 229:60-65, 1975.
35. Stella A., R. A. L. Dampney, R. Golin and A. Zanchetti. Afferent vagal control of renin release in the anesthetized cat. *Circ. Res.* 43: Supp 1 I-107-I111, 1978.
36. Taher M. S., L. G. McLain, K. M. McDonald, R. W. Schrier. Effect of beta adrenergic blockade on renin response to renal nerve stimulation. *J. Clin. Invest.* 57:459-465, 1976.
37. Thames M. D., Zubair-H1-Hassan, N. C. Brackett, R. R. Lower and H. A. Kontos. Plasma renin responses to hemorrhage after cardiac autotransplantation. *Am. J. Physiol.* 221:1115-1119, 1971.
38. Thames M. D. Reflex suppression of renin release by ventricular receptors with vagal afferents. *Am. J. Physiol.* 233:H181-H184, 1977.
39. Thames M. D., M. Jarecki and D. E. Donald. Neural control of renin secretion in anesthetized dogs. Interaction of cardiopulmonary and carotid baroreceptors. *Circ. Res.* 42:237-245, 1978.
40. Thames M. D. and G. F. DiBona. Role of renal nerves in renin release. *Fed. Proc.* 37:743, 1978.
41. Ueda H. H. Yasuda, Y. Takabatake, M. Iizuka, T. Iizuka, M. Ihori, M. Yamamoto, and Y. Sakamoto. Increased renin release evoked by Mesencephalic stimulation in the dog. *Jap. Heart J.* 8:498-506, 1967.
42. Vander A. J. Effect of catecholamines and the renal nerves on renin secretion in anesthetized dogs. *Am. J. Physiol.* 209:659-662, 1965.
43. Vander A. J. Control of renin release. *Physiol. Rev.* 47:359-382, 1967.
44. Yun J. C. H., C. S. Delea, F. C. Barter and G. Kelly. Increase in renin release after sinoaortic denervation and cervical vagotomy. *Am. J. Physiol.* 230:777-783, 1976.
45. Zambraski, E. J., G. F. DiBona and G. J. Kaloyanides. Effect of sympathetic blocking agents on the antinatriuresis of reflex renal nerve stimulation. *J. Pharmacol. Exp. Ther.* 198:464-472, 1976.
46. Zehr J. E., J. A. Hasbargen and K. D. Kurz. Reflex suppression of renin secretion during distension of cardiopulmonary receptors in dogs. *Circ. Res.* 38:232-239, 1976.
47. Zehr J. E. and E. O. Feigl. Suppression of renin activity by hypothalamic stimulation. *Circ. Res.* 32:Suppl 1 1-17 – 1-27, 1973.

$15,000 PRIZE ESTABLISHED IN BIOENGINEERING

The new Polytechnic/Wunsch Prize in Biomedical Engineering has been announced by George Bugliarello, President of Polytechnic Institute of New York.

Consisting of $15,000, the prize will be given for a major contribution to human health in which engineering methods have been used to solve medical problems.

The Prize was established by Dr. Joseph W. Wunsch, President of Silent Hoist and Crane Company, Brooklyn, N.Y., and a 1917 graduate of Polytechnic. The first award will be presented in the Spring of 1980. Deadline for nominations is November 1, 1979.

The Polytechnic/Wunsch Prize Committee includes Prof. William B. Blesser, Dept. of Mechanical and Aerospace Engineering, Polytechnic; Dr. Jack Jacobs, Dept. of Biomedical Engineering, Northwestern University; Dr. Richard Johns, Biomedical Engineering Dept., Johns Hopkins University Medical School; Dr. Herman P. Schwan, Dept. of Biomedical Engineering, University of Pennsylvania; APS member Dr. F. Eugene Yates, Dept. of Biomedical Engineering, University of Southern California; and Dr. Bugliarello.

The Committee invites nominations from inidviduals in engineering and medicine in the United States and abroad. Forms may be obtained by writing: Polytechnic/Wunsch Prize Committee, Polytechnic Institute of New York, 333 Jay St., Brooklyn, NY 11201.

NASAL AIRWAY RESISTANCE: ITS MEASUREMENT AND REGULATION*

LYLE H. HAMILTON
Department of Physiology, The Medical College of Wisconsin, Milwaukee, Wisconsin 53226 and the Research Service, Veterans Administration Medical Center, Wood (Milwaukee), Wisconsin 53193

Classically described functions of the nose are largely those related to olfaction and to protection of the lung. Respiratory physiologists tend to consider the latter as being more important, but some consequences of olfaction are more interesting, and have in the past played an essential role in survival of the individual (providing protection against enemies and guiding territorial identification) and of the species (affecting sexual behavior and aiding family identity). Man does not use olfaction for all of these purposes, although some aspects of their vestiges appear to still be active. For example, consider the basic drive behind the use of perfume by women and its acceptance by men.

Understanding the functions of the nose or its physiological control does not explain the need for the observed labile nature or exquisite control of airway caliber. Such variability might be concerned with providing an increased surface area or increased air turbulence for more efficient filtration, heat exchange or humidification, but these probably could have been maximized more efficiently by another mechanism without a complicated physiological control system. The question of whether such a system is required for the maintainance or rejuvenation of the mucous lining of the nose has not been answered in the major physiological literature.

Most physiological control systems are concerned with the conservation of energy or with an increase in the efficiency of the system. Active constriction of vascular channels conserves energy by adjusting regional blood flow to make it appropriate for regional metabolic needs. The physiologic control of bronchi results in a more even distribution of $\dot{V}_A/\dot{Q}_C$ throughout the lung. No such consequence is obvious from an increase in R_n. For the nose to perform its functions, air must flow through, and too little is known about airflow patterns in the nose to assign a benefit to increased total R_n. Furthermore, no adequate explanations have been provided for observed unilateral changes in R_n or for reflex alterations in total R_n (both demonstrated to be physiologically induced).

Fluid mechanics applied to nasal airflow.

Changes in nasal geometry can be detected indirectly by determinging the fluid mechanical resistance to gas flow. The resistance can be calculated from measurements of inflow pressure, outflow pressure and flow rate, and is based on an engineering equation called the "mechanical energy balance":

$$P_i - P_o = \Delta P = \rho \frac{\dot{V}^2}{2}\left[\frac{1}{A_o^2} - \frac{1}{A_i^2}\right] + \Sigma\Lambda \qquad [1]$$

where P_i = inflow pressure
P_o = outflow pressure
ΔP = driving pressure
ρ = gas density
$\dot{V}$ = gas flow rate
A_o = exit cross-section area
A_i = entrance cross-section area
$\Sigma\Lambda$ = sum of the serial mechanical energy losses due to frictional or viscous effects

Particularly for the measurement of mechanical energy losses for nasal airflow, the first term on the right side of equation [1], which describes the change in kinetic energy of the gas in terms of differences in inflow and outflow cross-sectional areas, can be ignored. This leaves the apparently more simple equation:

$$\Delta P = \Sigma\Lambda \qquad [2]$$

The term on the right side of equation [2] represents a complicated function of the gas physical properties, the gas flow rate and the geometry of the flow passages. To determine the functional (applicable) form of equation [2], the fluid mechanics of the gas flow must be considered. The first consideration is related to whether the flow is laminar or turbulent. Reynolds number provides a criterion for determining whether the flow is laminar or turbulent:

$$Re = {}^{4}\dot{V}/\nu\pi d \qquad [3]$$

where Re = Reynolds number
$\dot{V}$ = flow rate
ν = kinematic viscosity = η/ρ = viscosity/density
d = diameter of conduit

When Re <2000 for flow in a smooth bore conduit, the pattern of flow will be streamline, i.e., laminar. For laminar flow, the mechanical energy losses are defined by Poiseuille's law as:

$$\Lambda_{lam} = \Delta P = 8\eta(L/\pi r^4)\dot{V} \qquad [4]$$

where Λ_{lam} = mechanical energy loss for laminar flow
L = length of conduit
r = radius of conduit

Combining the physical characteristics of the gas and the geometry of the flow conduit into a single constant, K_{lam}, leads to:

$$\Delta P = K_{lam}\dot{V} \qquad [5]$$

When Re >2000, turbulent flow develops. This type of flow involves random bulk mixing of the gas in the stream, so smooth streamline flow no longer exists. The mechanical energy loss for turbulent flow in a smooth straight tube of uniform cross-sectional area, based on the Blasius friction factor, leads to the equation:

$$\Lambda_{turb} = \Delta P = \frac{4L}{d}\left(\rho\frac{v^2}{2}\right) f \qquad [6]$$

where Λ_{turb} = mechanical energy loss for turbulent flow
v = velocity
f = Blasius friction factor
= $0.0791\ Re^{-0.25}$

*Presented as a tutorial paper at the Fall Meeting of the American Physiological Society, St. Louis, MO. October 1978

Equation [6] can be simplified:

$$\Lambda_{turb} = \frac{0.24\ L\rho\ 0.75\eta\ 0.25\ \dot{V}1.75}{d\ 4.75} \quad [7]$$

The physical characteristics of the gas and the geometry of the flow conduit can again be combined into a new constant so the mechanical energy loss for turbulent flow in a smooth tube is:

$$\Delta P = K_{turb}\ \dot{V}^{1.75} \quad [8]$$

The kinematic viscosity of the air at 20°C is 0.149 cm^2/sec. From equation [3] it can be calulated that Re would be 2136 for a flow of 0.25 L/sec through a conduit having a diameter of 1 cm. Thus, with the irregular shape of the nasal airway and the fact that at least some portion of it has a cross-sectional area equivalent to or smaller than that of a conduit with a diameter of 1 cm, there will be turbulence in a normal nose at relatively low flow rates during quiet breathing.

For conduits which have continuously varying cross-sectional areas, which are not hydrodynamically smooth, which branch and converge, and which change directions abruptly, it is expected from fluids engineering considerations that the actual mechanical energy losses due to turbulent flow are "enhanced" due to a higher degree of turbulence in the gas stream. Under this condition, the Blasius friction factor is not applicable and the mechanical energy loss is proportional to the square of the flow:

$$\Delta P = K_{turb(e)}\ \dot{V}^{2.0} \quad [9]$$

The mechanical energy losses described by equations [5], [8] and [9] occur serially throughout the nasal passages (flow at a given point is either laminar or turbulent and the geometry of the conduit at that point will affect the turbulence level so it may or may not be enhanced). Because the total pressure drop is the sum of the series pressure differences, equation [2] can be written in a general form as:

$$\Delta P = \left[\Sigma K_{lam}\right]\dot{V} + \left[\Sigma K_{turb}\right]\dot{V}^{1.75} + \left[\Sigma K_{turb(e)}\right]\dot{V}^{2} \quad [10]$$

Most respiratory physiologists assume that the geometry of the nasal passage is sufficiently irregular to provide a highly turbulent flow, so equation [10] is usually simplified and presented in the more familiar form known as Rohrer's equation:

$$\Delta P = K_1\dot{V} + K_2\dot{V}^2 \quad [11]$$

where K_1 represents ΣK_{lam} and K_2 represents $\Sigma K_{turb(e)}$. The relative sizes of K_1 and K_2 express the relative contributions of laminar and turbulent flow to the total energy loss. Since they depend on the geometry of the flow passages, it can be expected that changes in the magintude of K_1 and K_2 reflect changes in the geometry of the flow passages. That is, if the gas composition remains constant (e.g., humidified air at body temperature), changes in the magnitude of $\Delta P/\dot{V}$ evaluated at a specific flow rate will reflect changes in the geometry (e.g., diameter) of the nasal airway as they affect K_1 and K_2, since:

$$\Delta P/\dot{V} = K_1 + K_2\dot{V} = R_n \text{ (with V fixed)} \quad [12]$$

Resistance calculations.

The calculation of R_n by the application of Ohm's law is meaningful as long as it is calculated at a fixed flow rate for air breathing, since $\Delta P/\dot{V} = K_1 + K_2\dot{V}$.

The fluid mechanical analogy of Ohm's law for electricity (resistance = Voltage/current) is expressed for R_n as:

$$R_n = \Delta P/\dot{V} = K_1 + K_2\,\dot{V}_{fixed} \quad [13]$$

where R_n = nasal airway resistance, cm $H_2O \cdot L^{-1}$ sec^{-1}.
Of course, R_n will be different at different values for $\dot{V}$, but since R_n is related to K_1 and K_2, it reflects the nasal geometry when measured at a given flow rate.

As in the electrical analogue, fluid mechanical resistances in series are additive. For instance, total resistance for air movement to and from the lung is the sum of the upper and lower airway resistances. That is,

$$R_{tot} = R_n + R_a \quad [14]$$

R_{tot} = total airway resistance

R_a = lower airway resistance

To calculate the total fluid mechanical resistance for two passages in parallel, such as the left and right nasal passages, parallel resistance formulas can be applied.

$$1/R_n = \frac{1}{R_\ell} + \frac{1}{R_r} \quad [15]$$

$$R_n = \frac{1}{\frac{1}{R_\ell} + \frac{1}{R_r}} \quad [16]$$

$$R_n = \frac{R_\ell \times R_r}{R_\ell + R_r} \quad [17]$$

It is important to stress that for the combined resistances to be meaningful, the two resistances (either in series or in parallel) must be measured at the *same flow rates.*

Methods for measuring R_n.

There are numerous empirical methods for measuring R_n. Many are indirect indices presumed to be correlated with R_n, but most have not gained widespread acceptance because they are not based on the simultaneous measurement of driving pressure and the consequent airflow.

A description will be made of three methods for calculating R_n, based on measuring the pressure-flow relationship for nasal airflow during breathing under precisely defined conditions.

Posterior rhinometry is the most widely used technique (5,7,13,16,22-24) (Fig. 1). A modified SCUBA mask is usually used to hold a pneumotachometer for the measurement of nasal airflow. This mask is employed in order to assure a tight seal around the face without touching the nose, which might result in a reflex change in R_n. The ΔP is measured with a differential pressure transducer, one side of which measures pressure in the mask (outside the nose) and the other side is connected to a mouthpiece or oral catheter for measuring oropharyngeal pressure. The pressure and flow can be recorded on a strip-chart recorder from which the R_n may be calculated at a specific flow rate by using equation [13]. A more conventional technique is to display the ΔP-$\dot{V}$ relationship as an X-Y plot on an oscilloscope screen from which $\Delta P/\dot{V}$ is measured and averaged for multiple breaths.

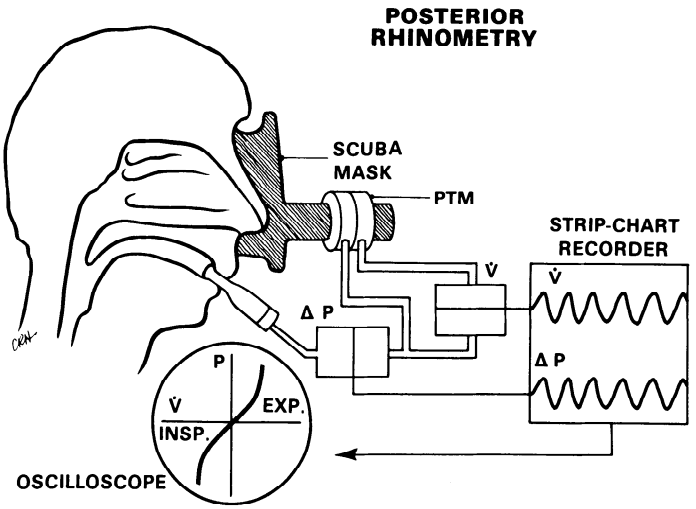


Fig.1. Diagram illustrating the principle of posterior rhinometry for the measurement of nasal airway resistance.

Anterior rhinometry is an alternate method of measuring R_n. It is not widely used, but, in practice, has the advantage of requiring less training by the subject (J. T. Connell, personal communication). The method is illustrated in Fig. 2. One nostril is occluded by a connector to a pressure transducer. The pressure at the nasopharynx is measured through that side while air moves through the unoccluded nostril during quiet breathing. Unilateral airflow is measured with a pneumotachometer placed against the patient's nostril. After the pressure-flow relationship for one side is recorded, the two transducers are reversed so the resistance of the other side can be measured. The two resistances are added by applying the parallel resistance equation [17] to obtain total R_n. It should be reemphasized that the pressure must be measured at the same flow rate on both sides for the calculated value of total R_n to be quantitatively exact.

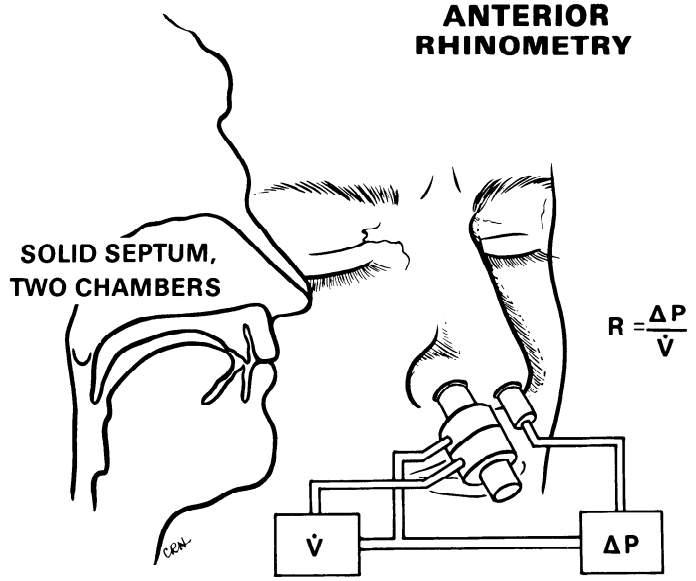


Fig. 2. Location of pressure and flow transducers for the measurement of unilateral nasal airway resistance by the technique of anterior rehinometry.

A third method for measuring R_n, based on pressure-flow measurements during the breathing cycle, uses the body plethysmograph. This technique is more commonly employed in pulmonary function laboratories to measure lower airway resistance, but it can be used for R_n by applying the series resistance equation [14] (1,18,19). Total resistance at a selected airflow rate is measured with the body plethysmograph during nose breathing. Next, lower airway resistance is measured at the same airflow rate during mouth breathing. Since series resistances are additive if measured at the same flow rates, the difference between total and lower airway resistance is nasal airway resistance.

In 1973, Nolte and Lüder-Lühr (18) showed a good correlation between R_n measured by body plethysmography and by posterior rhinometry. V̇alues for R_n from anterior rhinometry were more variable, and they did not recommend that method for measuring R_n.

For either anterior or posterior rhinometry, the most common method for calculating R_n is the oscilloscope tracing. Four approaches (with minor variations) are widely used (Fig. 3).

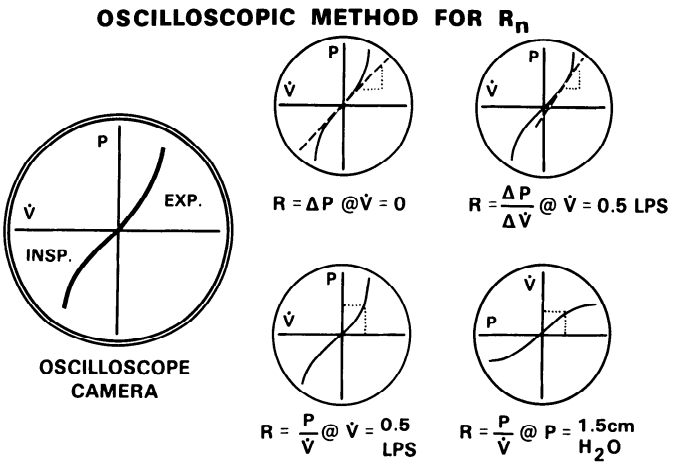


Fig. 3. Displays of **ΔP** and V̇ on the oscilloscope screen to calculate R_n by different procedures. See text for discussion.

The slope of the **ΔP/V̇** curve at the intercept (where ventilation is zero) is presumed to be a measure of R_n at laminar airflow, as seen in equation [13]. This technique is not widely used, although it has been supported by at least two laboratories which have made important contributions in this field (17,23). Its disadvantage is that the value for R_n is small, and changes associated with nasal congestion are less than with other methods. Accuracy may not be compromised, but the measurements must be made carefully to keep errors proportionately small.

Solomon and co-workers (University of Michigan) justified measuring the slope **dΔP/dV̇** (25). They (24) calculated the slope at a flow rate near 0.5 L/sec (35 L/min) (Fig. 3, upper right panel). These investigators argued that the calculation represents the true resistance for turbulent flow. Unfortunately, measuring the slope, **dΔP/dV̇**, at a specific V̇ does not measure R_n, but expresses the rate of change of R_n with V̇. Its usefulness in describing changes in nasal geometry is not clear from fluid mechanics considerations. The Michigan group has apparently changed to the measurement of the slope at the intercept (17), but at least one laboratory with which I am familiar still measures the slope of **dΔP/dV̇** at 0.5 L/sec airflow.

A widely used method measures R_n by dividing the driving pressure by the airflow rate at a flow rate of 0.5 L/sec (3,13,16). This is R_n as defined by Ohm's law in equation [13]. It reflects the energy required to produce the flow rate required for normal breathing and is related to the geometry of the nasal passages, as shown by fluid mechanical considerations. Therefore, it has some physiological as well as physical meaning.

The fourth variation for the calculation of R_n (Fig. 3) is the calculation of **ΔP/V̇** at a constant pressure. Both 1.0 (2) and 1.5 (J.T. Connell, personal communication) cm H_2O have been used, at which values flow rates slightly greater than 0.5 L/sec will be seen with normal R_n. The advantage of this method is that the

end-point can be reached by all subjects, including those who are congested to such a dgree that flow rates of 0.5 L/sec could not be achieved. It is used more frequently with anterior rhinometry, with the common pressure divided by the sum of the flow rates from both sides to provide a measure of bilateral R_n. Unfortunately, total R_n is not a meaningful value if the flow is different for the right and left sides, since R_n is a function of $\dot{V}$ as well as of K_1 and K_2, as seen in equation [12]. Such inequality of flow through both sides of the nose is a common finding during nasal congestion, so some limitation exists for the quantitative accuracy of R_n calculated by this method.

Some investigators have neglected to specify the flow rate at which R_n was measured (10, 22), or indicated that R_n was measured at peak flow rates during quiet breathing (13, 15), which would be variable if the degree of nasal congestion changed.

Many (if not most) investigators display the $\Delta P/\dot{V}$ curve on the oscilloscope with ΔP on the abscissa, since flow depends on the ΔP generate, and $\dot{V}$ is the dependent variable in that context. However, since flow is in the denominator of the equation and the resistance is defined for a fixed flow rate, a more appropriate display would be for $\dot{V}$ to be on the abscissa. The $\Delta P/\dot{V}$ curves are presented in that form in Figs. 3 and 4.

Figure 4 demonstrates the calculation of R_n by three accepted methods on a series of oscilloscope tracings of $\Delta P/\dot{V}$. They represent intermittent measurements of R_n over a 12-1/2 h period for a patient with untreated allergic rhinitis during natural exposure to ragweed pollen. The most important point to make from the Figure is that there is a lack of interchangeability among the methods. There is also a lack of precision for the measurement when multiple tracings are made on a single frame. A permanent record requires taking a photograph of the oscilloscope screen, which may be slow, awkward and expensive. Greatest accuracy would require a photograph for each breath, which borders on the impractical if changes in R_n with time are required.

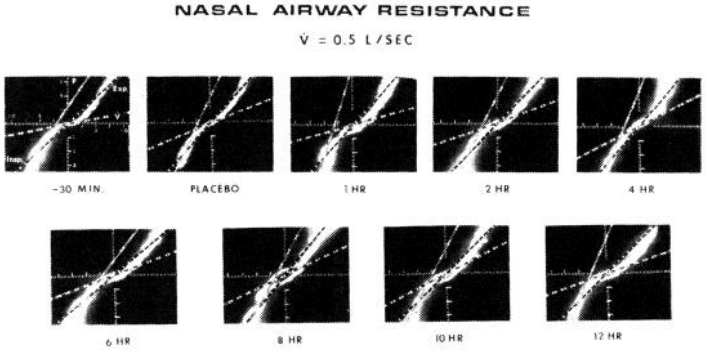


Fig. 4. R_n at 0.5 L/sec flow calculated from oscilloscope tracings by three techniques demonstrated in Fig. 3. For discussion, see text.

To improve the method for measuring R_n, we developed a nasal airway resistance computer (12) which records R_n for each breath (expiration and inspiration) at a preselected flow rate and on a continuous basis. The display of expiratory, inspiratory and continuous R_n, plus the primary pressure and flow signals, are presented in Fig. 5. The data in this figure are from the same study as that shown in Fig. 4. This was possible because ΔP and $\dot{V}$ are routinely recorded on magnetic tape in our laboratory and are available for alternate methods of analysis.

Inspection of the records in Fig. 5 shows that there is some variability from breath-to-breath and from hour-to-hour in R_n. Some additional observations can be made. Differences between expiratory and inspiratory R_n were observed at higher flow rates at some of the time periods (lower tracing), even when no major differences were seen at lower airflow rates (upper two tracings) for the same breaths.

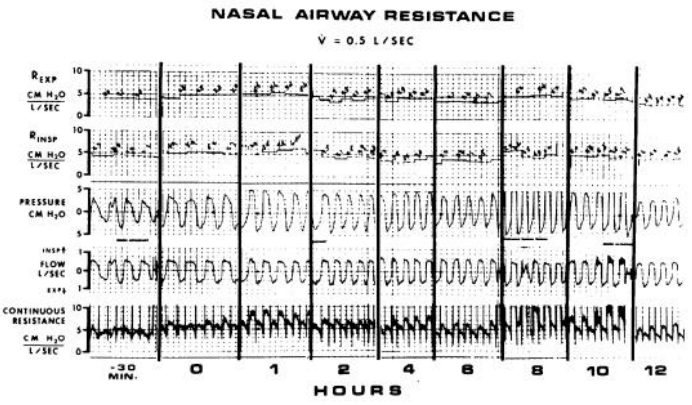


Fig. 5. Display of expiratory and inspiratory R_n at 0.5 L/sec flow rate, pressure and flow signals, and a record of continuous R_n (at all flow rates) for the same subject used for Fig. 4. The recording was made from the output of a nasal airway resistance computer (12).

Differences between expiratory and inspiratory R_n were described by Bridger and Proctor in 1970 (3). They described a "flow-limiting segment" (FLS) which functioned like a Starling resistor during maximal inspiratory effort. It is usually located at the proximal end of the nasal "valve," 0.5 to 1.0 cm deeper in the nose than the ostium internum, which is the narrowest part of the nasal passage. They also proposed that as the inferior turbinate fills with blood it may swell across the FLS and reduce maximal flow (increasing inspiratory R_n at higher $\dot{V}$). This might explain some of the variability in the relationship between expiratory and inspiratory R_n at peak $\dot{V}$ (Fig. 5).

Additional characteristics of R_n change are shown in Fig. 6, which is the response over a 3-h period to phenylephrine nasal spray, with R_n measured at 0.25 and 0.5 L/sec airflow at each time period. The data suggested a duration of effect which was shorter at 0.5 L/sec airflow than at 0.25 L/sec in both expiratory and inspiratory R_n for this subject, although that is not a general finding. Again, differences between expiratory and inspiratory R_n at higher flow rates were seen at some time periods even though similar differences were not seen at low flow rates. Some of the difference was due to a higher peak $\dot{V}$ during inspiration, suggesting that the FLS was not responsible, but sometimes peak $\dot{V}$ was comparable during expiration and inspiration and peak R_n values were still different (at +120 and +180 min). The importance of establishing a standardized flow rate for the measurement of R_n is emphasized with this Figure.

As with other scientific observations, statistical analyses are required to establish the validity of R_n changes. Work to be published has demonstrated that R_n data from normal subjects, as well as from those with nasal congestion, are consistently skewed to the right (toward high values) on a frequency plot. However, the logarithms of R_n were shown to be normally distributed. Furthermore, the response to a nasal decongestant (R_n at control time minus R_n after medication) was also skewed, but the logarithm of the response was not. This means that statistical analyses must be performed on the logarithm (or some other normally distributed function) of R_n rather than on the R_n value directly.

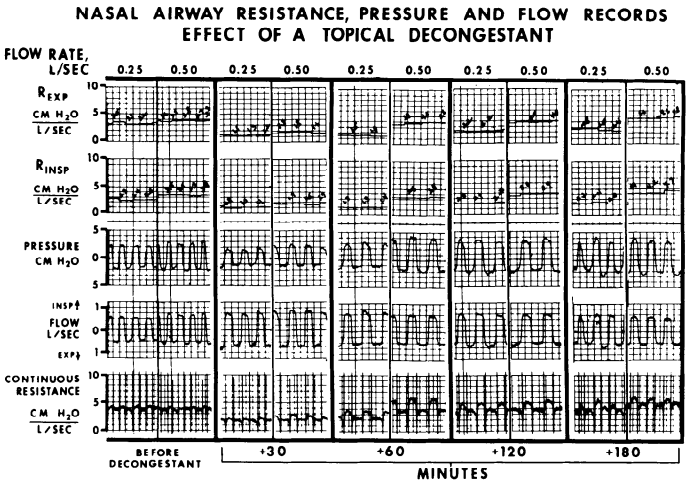


Fig. 6. Records from the nasal airway resistance computer for expiratory and inspiratory R_n at 0.25 and 0.5 L/sec airflow, ΔP and $\dot{V}$, and R_n at continuous flow from a subject with nasal congestion due to an upper respiratory infection before and up to 3 h after the topical application of phenylephrine nasal decongestant spray.

Standardizing the methodology for R_n.

Valid conclusions about the efficacy and duration of action of nasal decongestants can be drawn with data from any of the oscilloscopic methods described above, as long as it is correctly collected and properly analyzed. However, for the data to be interchangeable among investigators, it will be necessary to adopt a standard method for the measurement of R_n. This will occur when the leaders in the field insist on the kind of standardization leaders of other fields have previously demanded. The variety of methods now in use has led to a lack of confidence in the measurement, since the values for R_n from one laboratory may have no relationship to the values reported from another laboratory. The natural bias displayed by the developers or users of a "preferred" method may make it more difficult to convince workers in the field that it is important to standardize the method for measuring R_n. The nasal airway resistance computer (12) can be used to measure R_n at any desired flow rate, and having pressure and flow records on magnetic tape permits the careful analysis of tracings at multiple flow rates (other than at flow near zero). Such work should guide the definition of a standard method. There should be room for both anterior and posterior rhinometry, but there is little justification for not standardizing such variables as flow rates, the use of inspiration or expiration, and the mathematical form for the expression of R_n.

Several European investigators, including Spoor in Leiden (27), Nolte and Lüder-Lühr in Germany (18) and Dallimore and Eccles in Wales (8) have proposed that the pressure-flow relationship described for turbulent flow would be more appropriate for R_n since at least some turbulence exists for most of the breathing cycle. Our nasal airway resistance computer has recently been modified by the addition of another channel which will calculate R_n assuming that all flow is turbulent. The output of the analogue divider (continuous $\Delta P/\dot{V}$) is divided by $\dot{V}$ to provide a continuous signal for $\Delta P/\dot{V}^2$. Preliminary data suggest that many of the breathing cycles from subjects with nasal congestion have a nearly constant value for R_n calculated as $\Delta P/\dot{V}^2$, at least through the range of $\dot{V}$ for normal breathing. This supports the previous report of Spoor (27) who recorded $\dot{V}^2/\Delta P$ as nasal "conductivity," comparable to the reciprocal of R_n. However, other breaths which were analyzed with this technique did not provide a constant value for $\Delta P/\dot{V}^2$ and suggested that the denominator should more correctly have been between $\dot{V}^{1.25}$ and $\dot{V}^{1.75}$. It was demonstrated by Drettner in 1961 (9) that ΔP was related to $\dot{V}^{1.7}$ in the range of quiet breathing, and on that basis he concluded that most of the nasal airflow was turbulent. Such analyses may provided more information about the nature of R_n, and work is just beginning in this area using an available PDP/11 computer. A definitive description of relationship between driving pressure and flow rate, and information about factors which affect that relationship, will hopefully emerge. Of course, it should not be necessary to modify the currently used equations for R_n if a standard *single* flow rate is adopted. There is a difference between (a) adopting a valid method for measuring R_n to evaluate changes in nasal patency, and (b) developing methods which will provide new information about the determinants of R_n and the physiology related to changes in R_n.

Mechanism for R_n change

The mechanism for increasing R_n is involved with increasing the volume of blood in venous plexi located under the mucous membranes, particularly on the nasal septum and the turbinates. Because the nasal passages are surrounded by a rigid bony cavern, any increase in blood volume must reduce the cross-sectional area of the air pasages.

The vascular supply to the nose is supplied by the internal and external carotid arteries. The sinusoids, which are large capacitance vessels, are located in the circuit between the capillaries and the venules. The sinusoids are surrounded by circular and longitudinal smooth muscle, innervated by the autonomic nervous system. P-sympathetic stimulation leads to vasodilatation. Sympathetic fibers originate from the superior cervical ganglion and cause vasoconstriction of the nasal sinuses. Sympathetic innervation is dominant over the P-sympathetic effects on the plexi.

Reflex control of R_n

Several reflexes which are associated with changes in lower airway resistance have been demonstrated to also alter R_n.

In the same way that hypocapnia due to hyperventilation increases bronchial resistance, it was reported to cause an increase in R_n (8). Hypercapnia in response to rebreathing caused a decrease in R_n (8), as did inhalation of 8% CO_2 or breath-holding (22). Dallimore and Eccles (8) found a decrease in R_n as a result of exercise. They concluded that it was part of the general response to exercise and required a different stimulus than that seen with hypercapnia. Most investigators suggest that these responses are reflex in nature rather than being localized. The response to asphyxia in the anesthetized dog was abolished by cervical sympathetic denervation (28), although it did not affect the increased R_n observed during hyperventilation.

Both hot and cold thermal stimuli increase R_n. It was demonstrated by Salman et al. (23) that breathing either hot or cold air caused an increase in R_n. Martin and Tansy (16) demonstrated that either hot or cold water (not tepid water) held in the mouth also produced a transient increase in R_n.

A complicated reflex relationship apparently exists between upper and lower airway resistances. Sercer (a pioneer laryngologist from Yugoslavia) many years ago described an ipsilateral bronchoconstriction and a change in unilateral diaphragmatic activity when one side of the nose was stimulated mechanically. These studies were described to me by I. Padovan, a former student of Sercer. Ogura, from Washington University in St. Louis, is another academic laryngologist who has provided important data on the relationship between upper and lower airway resistance. He has shown that a progressive increase in R_n is accompanied

by an increase in lower airway pressure (19). His group also reported an increased laryngeal resistance (R_{lrx}) caused by experimental nasal obstruction (2). Lacourt and Polgar (14) reported that, in infants, an increase in R_n was accompanied by a decrease in R_{lrx}, so total airway resistance was not greatly changed. Spann and Hyatt (26) were unable to confirm any relationship between R_{lrx} and R_n change due to partially obstructed nostrils. Thus, no final conclusions can be drawn about the relationship between R_n and R_{lrx} although the concept of a reflex relationship between R_n and lower airway resistance has been well documented and is further supported by animal studies. Whicker and Kern (29) described a nasopulmonary reflex which resulted in increased lower airway resistance (R_{law}) after thermal (ice water) stimulus of the nasal mucosa in unanesthetized dogs. Allison et al. (1) reported that chemical stimulation of the nose (ether, ammonia or tobacco smoke) decreased R_{law} in rabbits and that it returned to the control level following bilateral cervical vagotomy.

Nasal cycling

The existence of nasal cycling is well known to investigators working in the field of nasal physiology. To my knowledge, it has not been well described in the general literature, so most physiologists who do not specialize in nasal studies are unaware of this surprising nasal phenomenon.

As illustrated in Fig. 7, which is a replot of data from Dallimore and Eccles (8), nasal cycling consists of a reciprocal change in R_n between right and left sides, with little or no change in total R_n. It is observed approximately 80% of the time, whether measured in the same individual or in the population, so it is intermittent in nature. When it occurs, it has a cycle duration which varies from 1/2 to 4 h, more commonly 2 to 3-1/2 h.

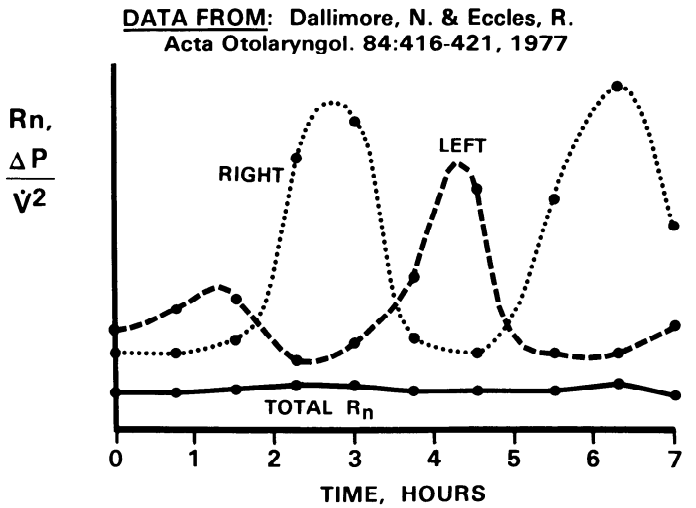


Fig. 7. Replot of data from Dallimore and Eccles (8) to demonstrate the constancy of total R_n during a period of nasal cycling in a normal subject.

According to most descriptions of nasal cycling, the first observations of the phenomenon were made in 1895 by Kayser in Germany and were confirmed in 1927 by Heetderks.

Early objective measurements of nasal cycling were reported by Ogura and Stokstead in 1958 (20), Connell in 1968 (6), and Principato and Ozenberger in 1970 (22). Some of the more recent reports have come from Dallimore and Eccles (8) and Eccles (11), who described careful studies of the phenomenon in humans and in animals.

Ogura and Stokstead (20) reported that variations in temperature and humidity caused the turbinates to respond with synchronous movements. Principato and Ozenberger (22) studied interruption of the cycle by the topical application of ephedrine. R_n failed to increase on one side during the period when ephedrine exerted an effect, but cycling reoccurred on schedule after the effect of the drug was gone. This suggested to them a central regulatory mechanism, unaffected by local stimuli. These investigators reported that the status of the cycle on one side had no effect on the opposite side. Connell (6), on the other hand, observed that contralateral decongestion followed congestion on one side, and most reports suggest that the relationship between the two sides is regulated centrally. In work with pigs, Eccles (11) reported that unilateral section of a cervical sympathetic nerve abolished the reciprocal change in R_n. It was suggested that sensory fibers may have a role in regulating R_n, with ipsilateral nerve section causing a bilateral disturbance.

While studies of nasal cycling are continuing, little progress has been made toward understanding this phenomenon. The stimulus is not known, other than the early observation by Ogura and Stokstead (20) that it was affected by variations in temperature and humidity. A further description of that effect has not been found in the literature. The cycle can be interrupted as described above, but methods for initiating the cycle or altering its period, for instance, have not been reported. Is the cycle related to saturation or fatigue of the mucous escalator which removes entrapped particulate matter? Would the period of the cycle be affected by the level of inhaled particles, or is there a CNS regulator which is independent of the condition of the mucosa? I am not aware of work being conducted in this specific area of nasal cycling, although attention is being given to this aspect of nasal physiology.

Nasal physiology is one of the fields of research which is still wide open for the im ginative investigator. Studies of the regulation of R_n offer an opportunity to describe new fundamental relationships. A new approach to studies of nasal cycling, for instance, might change the entire concept of autonomic control or uncover reflexes which have been heretofore not even suspected. Such areas offer the opportunity for young physiologists to become pioneers early in their careers. I recommend it to those who are still looking for an area where they can follow the beat of a different drum -- or even establish a new drum beat for others to follow.

ACKNOWLEDGEMENTS

The considerable effort expended by Dr. John H. Linehan, Professor of Mechanical and Biomedical Engineering at Marquette University, Milwaukee, in helping me understand the mechanical energy balance equations as they apply to nasal airflow is appreciated. The role of Mr. N. Thomas Christman in designing and constructing the nasal airway resistance computer and in helping in all aspects of our nasal studies has been invaluable. The technical assistance of Mrs. Judith Hoernke should also be acknowledged. She has developed the measurement technique to a fine art and helped collect the data without which this report would not have been prepared.

REFERENCES

1. Allison, D.J., T.P. Clay, J.M.B. Hughes, H.A. Jones and A. Shevis. Effects of nasal stimulation on total repiratory resistance in the rabbit (Abstract). *J. Physiol.* 239:23P-24P, 1974.
2. Aschan, G. Decongestion of nasal mucous membranes by oral medication in acute rhinitis. *Acta Otolarynogol.* 77:433-438, 1974.
3. Bridger, G.P., and D.F. Proctor. Maximum nasal inspiratory flow and nasal resistance. *Ann. Otol.* 79:481-488, 1970.

4. Butler, J. The work of breathing through the nose. *Clin. Sci.* 19: 55-62, 1960.
5. Cohen, B.M. Nasal airway resistance and effects of bronchodilator drugs in expiratory airflow disorders. *Respiration* 26: 35-46, 1969.
6. Connell, J.T. Reciprocal nasal congestion-decongestion reflex. *Trans. Am. Acad. Ophthalmol. Otolaryngol.* 72: 422-426, 1968.
7. Craig, A.B., M. Dvorak, and F.J. Mcillreath. Resistance to airflow through the nose. *Ann. Otol. Rhinol. Laryngol.* 74:589-603, 1965.
8. Dallimore, N.S., and R. Eccles. Changes in human nasal resistance associated with exercise, hyperventilation and rebreathing. *Acta Otolaryngol.* 84: 416-421, 1977.
9. Drettner, B. Vascular reactions of the human nasal mucosa on exposure to cold. *Acta Otolaryngol.* Suppl. 166, 1961.
10. Eccles, R. Cyclic changes in human nasal resistance to air flow (Abstract). *J. Physiol.* 272:75P, 1977.
11. Eccles, R. The domestic pig as an experimental animal for studies of the nasal cycle. *Acta Otolaryngol.* 85:431-436, 1978.
12. Hamilton, L.H., and N.T. Christman. Nasal airway resistance computer. *Larynogscope* 87: 1945-1950, 1977.
13. Hasegawa, M., and E.B. Kern. The human nasal cycle. *Mayo Clin. Proc.* 53: 28-34, 1977.
14. Lacourt, G., and G. Polgar. Interaction between nasal and pulmonary resistance in newborn infants. *J. Appl. Physiol.* 30: 870-873, 1971.
15. Martin, J., and M.H.F. Friedman. Nasal airway resistance and blood flow (Abstract). *Physiologist* 15: 209, 1972.
16. Martin, J.S., and M.F. Tansy. Thermal stimulation of the oral mucosa and nasal airway resistance. *J. Dent. Res.* 56: 1313-1322, 1977.
17. McLean, J.A., A.A. Ciarkowski, W.R. Solomon and K.P. Matherws An improved technique for nasal inhalation challenge tests. *J. Allergy Clin. Immunol.* 57: 153-163, 1976.
18. Nolte, D., and I. Lüder-Lühr. Comparing measurements of nasal resistance by body plethysmography and by rhinomanometry. *Respiration* 30: 31-38, 1973.
19. Ogura, J.H., and J.E. Harvey. Nasopulmonary mechanics - Experimental evidence of the influence of the upper airway upon the lower. *Acta Otolaryngol.* 71: 123-132, 1971.
20. Ogura, J.H., and P. Stokstead. Rhinomanometry in some rhinologic diseases. *Laryngoscope* 68: 2001-2014, 1958.
21. Ogura, J.H., M. Suemitsu, J.R. Nelson and S. Kawamoto. Relationship between pulmonary resistance and changes in arterial blood gas tension in dogs with nasal obsruction, and partial laryngeal obstruction. *Ann. Otol.* 82: 668-683, 1973.
22. Principato, J.J., and J.M. Ozenberger. Cyclical changes in nasal resistance. *Arch. Otolaryngol.* 91: 71-77, 1970.
23. Salman, S.D., D.F. Proctor, D.L. Swift and S.A. Evering. Nasal resistance: Description of a method and effect of temperature and humidity changes. *Ann. Otol.* 80: 736-743, 1971.
24. Solomon, W.R., J.A. McLean, C. Cookingham, G. Ahronheim and G.R. DeMůth. Measurement of nasal airway resistance. *J. Allergy* 36: 62-69, 1965.
25. Solomon, W.R., and A.W. Stohrer. Considerations in the measurement of nasal patency. *Ann. Otol. Rhinol. Laryngol.* 74: 978-990, 1965.
26. Spann, R.W., and R.E. Hyatt. Factors affecting upper airway resistance in conscious man. *J. Appl. Physiol.* 31: 708-712, 1971.
27. Spoor, A. On the nasal conductivity. *Pract. Otorhinolaryngol.* 29: 315-324, 1967.
28. Tatum, A.L. Effect of deficient and excessive pulmonary ventilaton on nasal volume. *Am. J. Physiol.* 65:229-233.
29. Whicker, J.H., and E.B. Kern. The nasopulmonary reflex in the awake animal. *Ann. Otol.* 82: 355-358, 1973.

STUDY IN GERONTOLOGY

The following courses are being offered as part of the 1979 Summer Institute for Study in Gerontology, sponsored by the Andrus Gerontology Center of the University of Southern California.

For further information and enrollment application, please contact: Summer Institute, Andrus Gerontology Center, University of Southern California, University Park, Los Angeles, CA 90007. (213) 741-6765

June 25 - June 29, 1979. Accessing Information Sources in Gerontology.
July 2 - July 13, 1979. Biological Processes and Aging.
July 16 - July 27, 1979. Physiology, Nutrition, and Aging.

XXXIII WORLD MEDICAL CONGRESS

The XXXIII World Medical Congress will be celebrated from October 21 to October 27, 1979 at the Hotel Macuto Sheraton in Caraballeda, Federal District, Venezuela.

For forms and further information write to:

Dr. Antonio Clemente H.
Chrmn, Scientific Meeting
La Asociacion Medica Mundial
33 Asamblea Medica Mundial
Carabelleda, Venezuela

EXTRACELLULAR NUCLEOTIDES IN EXERCISE: POSSIBLE EFFECT ON BRAIN METABOLISM*

TOM FORRESTER
Department of Physiology
St. Louis University Medical Center
St. Louis, MO 63104

Introduction

The roles that intracellular nucleotides play in cellular metabolism are well understood and formidable metabolic pathways controlled by nucleotides have been worked out in great detail. However the actions of nucleotides *extracellularly* have only recently come into prominence with the realization that these substances can exist, and have highly potent actions, outside the cell.

As long ago as 1929 Drury & Szent-Gyorgyi published a paper in *The Journal of Physiology* describing the action of adenosine triphosphate and derivatives when applied externally to the heart and blood vessels. They emphasized the great sensitivity of these tissues to the adenyl compounds. This might have prompted the immediate conclusion that there must exist nucleotide *receptors* to respond to the agonist nucleotide, a concept that has only now been put forward by Sattin & Rall (1970), Burnstock (1978) and others nearly fifty years later. Since then widespread actions of the nucleotides on many tissues have been described. The urgencies of World War II brought forward a significant report which largely summarized the extracellular actions of the nucleotides, particularly ATP, in the body organs. Much of this work is described by Green & Stoner (1950) who showed that circulating ATP could be responsible for the *wound shock* seen in battle casualties. The peripheral blood vessels seemed to dilate greatly and in some cases irreversibly when a large mass of tissue was destroyed. At this time Green & Stoner commented "that the problem was hindered by the lack of definition in the chemical methods available for estimating small changes in the body nucleotides." Little was published on extracellular activity of these substances until Pamela Holton (1959) demonstrated the presence of ATP in the effluent from rabbit ear artery associated with sensory nerve stimulation. Prior to this any physiological role for extracellular ATP had been regarded as highly unlikely, the general assumption being that an anion of such charge could not possibly pass across the cell membrane. However, with the development of more sensitive and rapid methods of ATP detection many studies have now been performed since then and many species have been used. A typical result is shown in Fig. 1.

This review will describe experiments demonstrating the release of ATP from skeletal muscle, cardiac muscle and active brain tissue. The effects of exogenously applied ATP to brain tissue will be discussed in relation to whole body exercise.

Release of ATP from active skeletal muscle.

Release of adenine nucleotides from active frog nerve and muscle *in vitro* was first noted by Abood, Koketsu & Miyamoto (1962) using indirect labelling methods. A direct bioassay system for ATP arose unexpectedly during a search for acetylcholine released from motor nerve terminals (Boyd & Forrester, 1968). When a solution bathing an indirectly stimulated frog sartorius muscle was perfused through a frog heart, a positive inotropic effect was produced. Fig. 2 shows the effect of such a solution on an isolated perfused frog heart beating against a constant peripheral resistance. There is an obvious similarity between the effect of the test solution and pure ATP. Adrenergic blockade of the heart with pronethalol and ergotamine did not affect the stimulatory effect of the muscle solution, thus ruling out the possibility that the stimulatory effect was produced by a catecholamine. Further tests of identification were employed. It was found that the stimulatory substance could be eluted into one fraction using molecular sieve chromatography (Sephadex G-25). An R_f value similar to that of ATP was obtained. This procedure involved testing the eluted fractions from the column on the very sensitive frog heart perfusion system. A concentration of as low as 10^{-9}M could be detected. The molecular sieving also removed the protein fraction, thus making the solution available for spectrphotometric analysis. Maximum absorption of light occurred at 265 nm (ph 7.1), probably indicating the presence of substances containing a purine ring. Incubation of the test solution with enzyme *apyrase* markedly reduced the stimulatory effect on the frog heart. Since apyrase catalyses the breakdown of nucleotide triphosphate to monophosphate, and monophosphate does not stimulate the frog heart, this provided strong evidence that the stimulatory substance contained a 'high energy' phosphate chain.

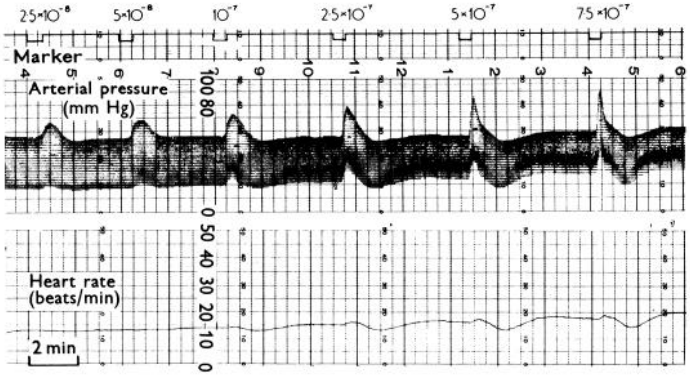


Fig. 1. The effect of graded concentrations of ATP solutions (g/ml) when perfused through a frog heart beating against a fixed peripheral resistance. There is a positive inotropic effect and a late increase in heart rate with the higher concentrations. (Boyd and Forrester, 1968, *J. Physiol, London).*

Finally, the test solution caused light to be emitted from firefly lantern extract, the pattern of light emission being similar to that produced by pure ATP. It was concluded that ATP, probably along with other nucleotides, was released from contracting skeletal muscle *in vitro.* At the time it seemed significant that no ATP could be detected when the muscles were stimulated indirectly, but curarized. In retrospect this did not indicate that *no* ATP came from active nerve terminals, but simply that the amounts released from that particular source did not achieve detectable levels in the bathing solution.

A justifiable criticism of this work was the possiblity that the ATP had as its source muscle fibers damaged during dissection. It had been noted, however, that the potassium levels in the solutions bathing the inactive muscle remained at control levels. Nevertheless it was decided to use a frog muscle preparation in

* Presented as a tutorial paper at the APS Fall Meeting in St. Louis.

which the hindlimb musculature is left intact and perfused through the abdominal aorta. This preparation was first developed by Dale and his colleagues during their search for acetylcholine released from motor nerve terminals. ATP was clearly demonstrated (Figs. 3,4) in the perfusate from indirectly stimulated hindlimb musculature, applying the tests for identification previously described (Forrester & Hassan, 1973).

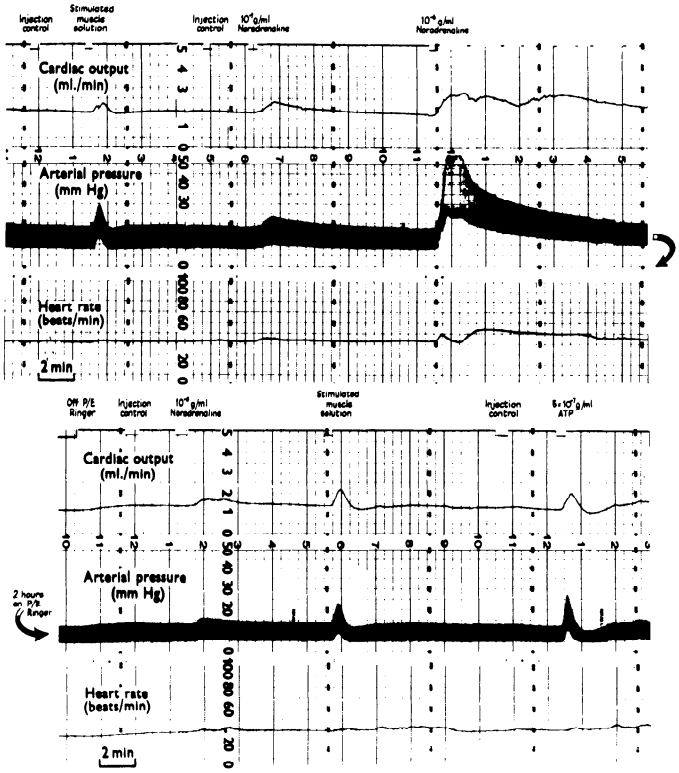


Fig. 2. Responses of a perfused frog heart to a solution in which a frog sartorius muscle had contracted and to solutions of norepinephrine and ATP before and after adrenergic blockade. Lower trace continues directly from upper trace. Heart was perfused for 2 hours with a Ringer's solution containing pronethalol hydrochloride, 10^{-6}g/ml, and ergotamine tartrate, 10^{-6}g/ml. Adrenergic blockade was sufficient to block the effect of norepinephrine almost completely. The action of the stimulated muscle solution (and ATP) remained unaffected. It indicates that the ATP contained in the muscle solution was acting "beyond" the adrenergic receptor. (From Forrester, 1967, Ph.D. Thesis, Glasgow).

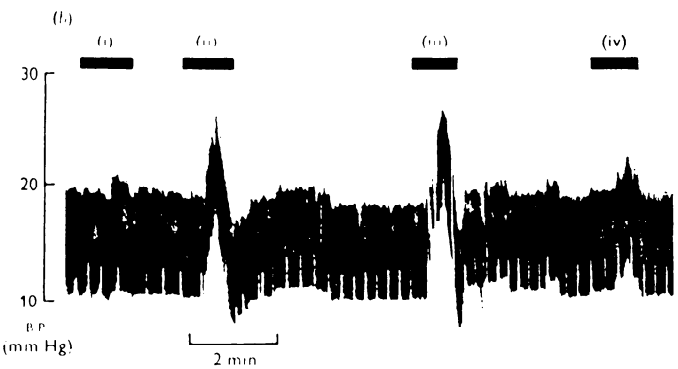


Fig. 3. Response of perfused frog heart to perfusate from frog hind limb muscles. Perfusate from (i): unstimulated hind limbs; (ii): limbs stimulated at 5 Hz.; (iii): response to ATP, 10^{-8}g/ml; (iv): sample (ii) after incubation with the dephosphorylating enzyme apyrase. Horizontal bar, time of perfusion (Forrester and Hassan, 1973, *J. Physiol., London*).

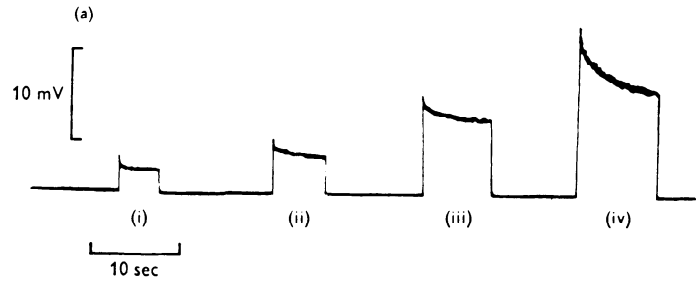


Fig. 4. Response of firefly extract to perfusate from frog hind limb muscles (i): perfusate from unstimulated hind limbs; note no decay of light signal; (ii), ATP, 10^{-8}g/ml; (iii) perfusate from limbs stimulated at 5 Hz.; note decay similar to that of pure ATP; (iv), ATP, 5×10^{-8}g/ml (Forrester and Hassan, 1973, *J. Physiol., London*).

At this juncture it was realized that ATP could have a role to play in the hyperemic response seen in skeletal muscle during exercise, since ATP is well known as a powerful vasodilator. Thus it was decided to apply these techniques of detection and identification to human peripheral blood despite the fact that human plasma contains enzymes capable of rapidly degrading ATP. When suitably diluted human plasma was perfused through a frog heart the same stimulatory response was seen, typical of ATP (Figs. 5,6). The amount of ATP in plasma from the venous blood of resting subjects (antecubital vein sample) ranged from 0.19 - 0.95 μg/ml (0.37 - 1.9 nmoles/ml). Approximately half of this amount was attributed to platelet damage. Simultaneous arterial and venous samples from four subjects at rest had mean concentrations of 0.19 μg/ml (0.37 nmoles/ml) and 0.70 μg/ml (1.3 nmoles/ml) respectively, indicating that the ATP was added to the blood on its way through the skeletal muscle bed. The concentration of ATP in the venous effluent from human forearm muscles performing a controlled amount of isometric exercise was measured (Forrester & Lind, 1969). Fig. 7 shows the results obtained from subjects performing 10% and 20% of their maximum voluntary contractions (MVC). Note that with the 20% MVC the concentrations rise steadily after the end of the contraction period, presumably indicating that as the post-exercise hyperemia diminished, the concentration will steadily rise if the musculature adds ATP to the venous effluent after contraction has ceased. With the 10% MVC a peak of concentration is evident, when post-exercise hyperemia was naturally not so great. It was established that the arterial levels remained low during and after the isometric exercies (Fig. 8). These results were soon substantiated by Parkinson (1973) who noted rises in blood levels of ATP, ADP and AMP occurring as long as five minutes after whole body exercise.

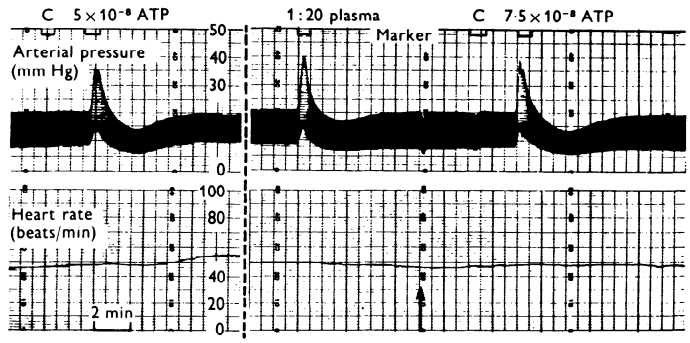


Fig. 5. Comparison of the action on a perfused frog heart of solutions of ATP (g/ml) and a diluted solution of fresh human plasma. Heart continuously perfused with Locke solution. C, control injection; vertical interrupted line, 25 min period; ↑, fall in perfusion pressure during flushing of residual plasma solution from perfusion system. The actions of plasma and ATP are almost identical. (Forrester and Lind, 1969, *J. Physiol. London*).

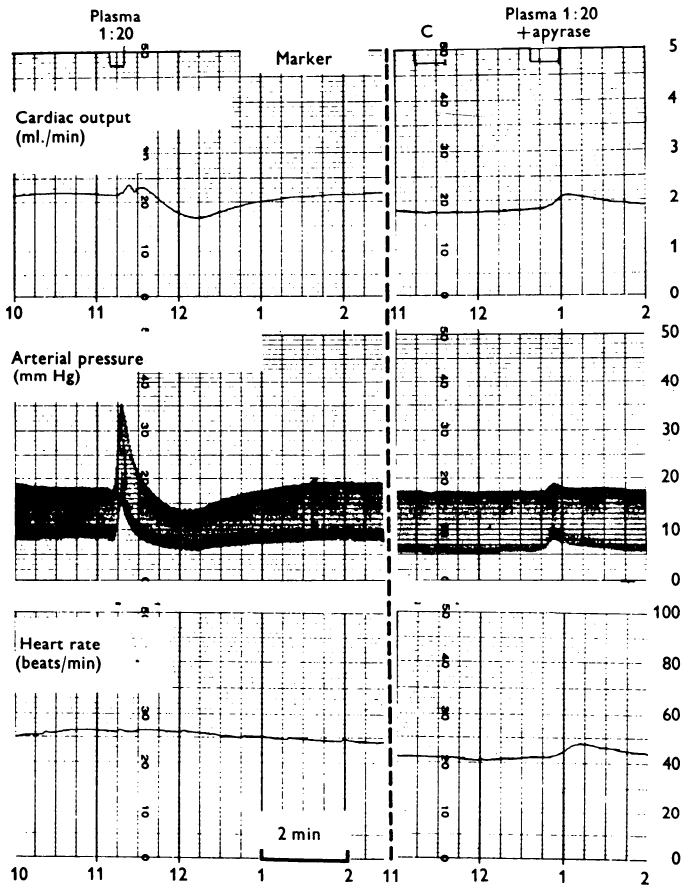


Fig. 6. The effect of a diluted plasma solution before and after incubation with apyrase on a perfused frog heart. Vertical interrupted line, 20 min period. After incubation with apyrase the same solution has a much reduced inotropic effect. The increase in cardiac output was caused by an increase in the heart rate. (Forrester and Lind, 1969, *J. Physiol., London*).

These results naturally led to the enquiry: is ATP released in sufficient quantities to satisfy the vasodilator requirements of active skeletal muscle? Previous studies on the effect of infused ATP on the circulation through human forearm musculature (Duff, Patterson & Shepherd, 1954) provided an opportunity to quantify the amounts of ATP released *in vivo* (Fig. 9). The main difficulty with a quantitative study of this sort is the fact that an increase in blood flow through exercising skeletal muscle has the effect of washing out and diluting the ATP to an unknown extent. One way round this difficulty is simply to occlude the arterial supply to the muscles during the period of exercise, and then gradually restore the flow which will then pass through the line of least resistance, that is, the dilated vessels in the skeletal muscle bed. Human subjects gripped a bar isometrically at 5% MVC in the presence of arterial (and venous) occlusion. This exercise is a mild one, and normally gives rise to an exercise hyperemia of only three times the resting flow (Lind & McNicol, 1967). Duff *et al* (1954) showed that a threefold increase in forearm flow could be produced by infusing ATP, 16 μg/min (30 nmoles/min), into the brachial artery. Figs. 10 & 11 show the results obtained in six experiments on four subjects. It is important to note the logarithmic ordinate scale, indicating a 10 - 100 fold increase in the concentration at the end of the four minute exercise period. These concentrations represent only a small fraction of the ATP orginally present because the rapid degradation in the bloodstream by plasma and blood elements could not be avoided. This factor would certainly diminish the concentrations of ATP infused by Duff *et al* (1954). A computation of the loss occurring was made and it was calculated that 7.5 - 10.5 μg/min (14-20 nmole/min) were released (Forrester, 1972). These amounts compare well with the 16 μg/min infused by Duff et al to produce the same threefold increase in flow (Fig. 9).

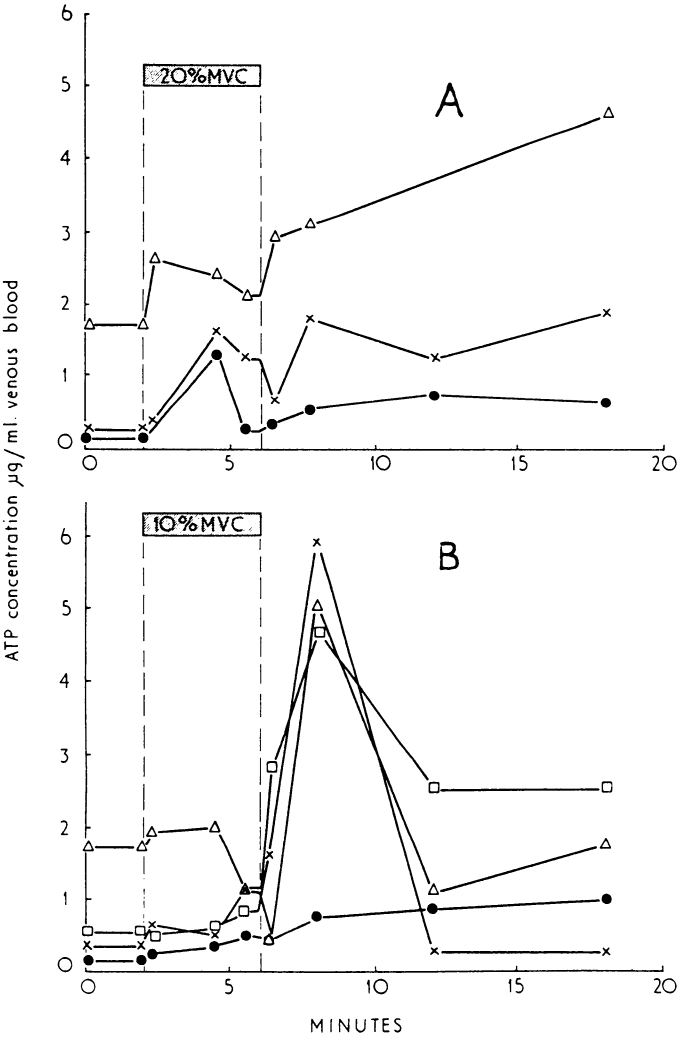


Fig. 7. The ATP concentration (μg /ml) in the venous effluent from human forearm muscle before, during and after 20% (A) and 10% (B) maximum voluntary contraction. Different symbols represent different subjects. Shaded bar indicates duration of contraction. Note the slow rise in concentration during the post-contraction phase in the 20% MVC (a tension eventually resulting in fatigue) in contrast to the sharp rise and fall obtained in the non-fatiguing 10% MVC. (Forrester and Lind, 1969, *J. Physiol., London*).

Release of ATP from myocardial cells in response to hypoxia

The findings with skeletal muscle *in vivo* encouraged further investigation using myocardial cells. The search for mechanisms of coronary vasodilatation has been going on for many years and is of obvious importance in view of the great morbidity associated with myocardial ischemia. Many substances have been implicated in the search for 'the vasodilator' (see review by Berne, 1964) but because of potency and/or lack of detection, none so far have been found satisfactory. The adenosine hypothesis put forward by Berne (1963) seems to be unsatisfactory on the grounds that aminophylline blocks the dilatory action of adenosine but not that of hypoxia (Afonso, Ansfield, Berndt & Rowe, 1972). An increase in the levels of ATP in the coronary sinus effluent of perfused guineapig hearts has been observed whenever the myocardium was made hypoxic (Paddle & Burnstock, 1974) but it was not certain whether the ATP came from nerves, vascular smooth muscle or myocardium (Fig. 12). The

use of adult rat heart cells isolated according to a method devised by Vahouny, Wei, Starkweather & Davis (1970), modified by C. A. Williams (1977) avoided many problems associated with whole heart preparations. The high ratio of surrounding fluid volume to cellular volume provides excellent conditions for oxygenation. No alteration in surrounding fluid volume occurs, thus avoiding the difficulty of having to estimate ATP concentrations in fluid coming from a vascular bed which is continuously dilating in response to hypoxia. The actual estimation of ATP remains free from both contaminating elements such as the blood platelets, and degrading elements, the blood ATPases. It was found that ATP, 0.34 μM/mg protein, was released from oxygenated cells, while 1.28 μM/mg protein was released within 30 seconds of rendering the cells hypoxic (Fig. 13). Fig. 14 shows the compiled results of the data. When hypoxic cells were restored to the oxygenated state the levels of ATP reverted to the previous low levels (Fig. 15). The amounts of ATP released were calculated to fall well within the range necessary for production of maximum vasodilatation of the coronary vascular bed. Continuous release of ATP from these cells supports the possibility that the tone of coronary vessels is a function of this release. It is of interest at this point to note that Giles & Wilcken (1977), working with dog heart, have shown that the response of the coronary blood flow to ATP was *not* changed by aminophylline.

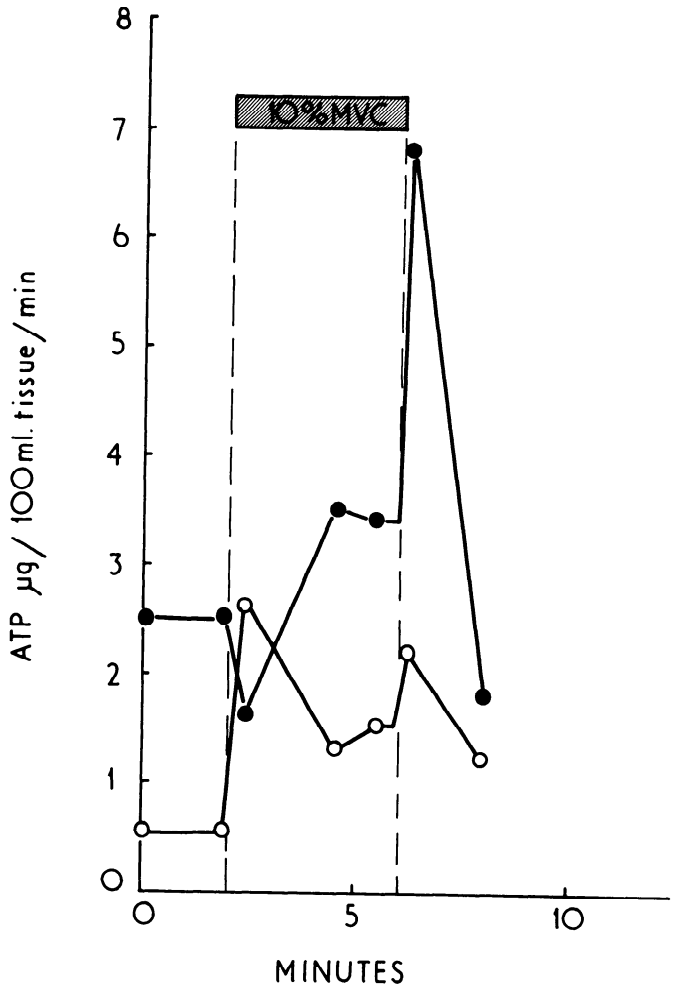


Fig. 8. Amounts of ATP measured in arterial (o) and venous (•) blood of one subject before, during and after a 10% MVC. Note the cross-over in first samples after onset of exercise. Arterial levels (from brachial artery) remain constant and below venous levels, indicating that the ATP was added to the blood in its passage through the exercising muscle. (Forrester and Lind, 1969, *J. Physiol., London*).

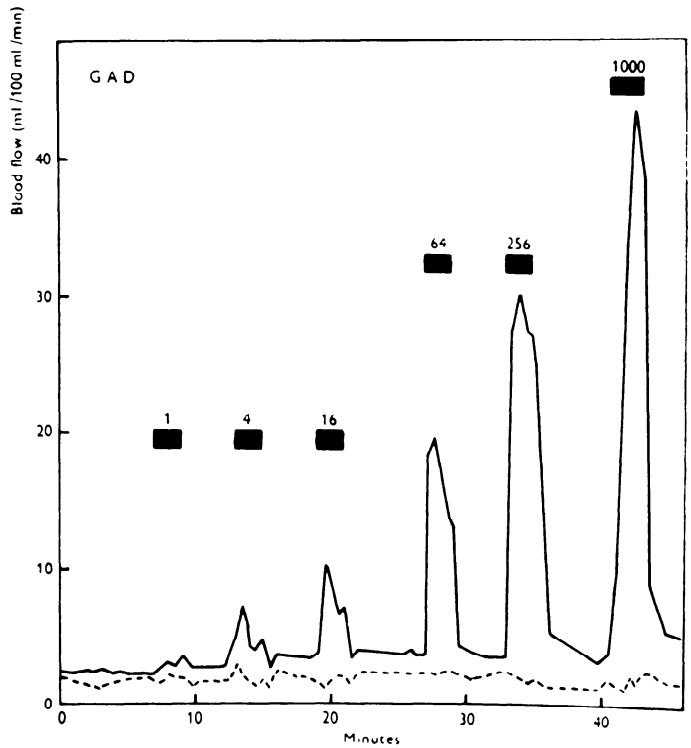


Fig. 9. The effect on forearm blood flow of various doses of magnesium ATP injected over 2-min periods into the brachial artery of a normal subject. Dotted line is control obtained from contralateral arm. Thick bars, times of perfusion with dose in μg/min. Note that 16 μg/min increases blood flow by about three times. (From Duff, Patterson and Shepherd, 1954, *J. Physiol., London*).

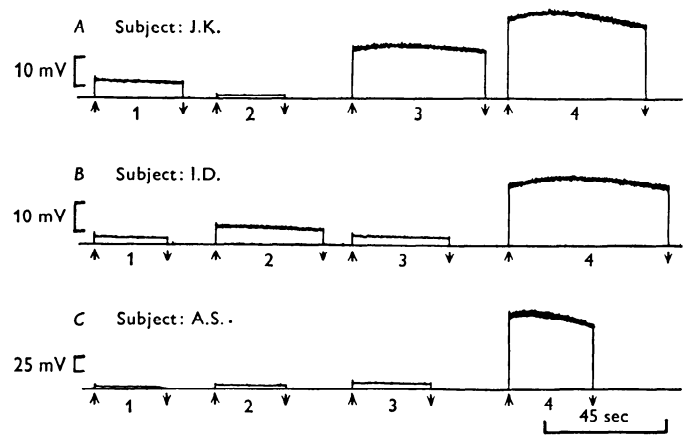


Fig. 10. Response of firefly extract to plasma samples from the forearms of three subjects, A, B and C. Sample 1 taken before onset of exercise (5% MVC); samples 2 and 3 taken during occlusion and exercise; sample 4 taken just after occlusions, exercise continuing. ↑, voltage switched on; ↓ voltage switched off. (From Forrester, 1972, *J. Physiol., London*).

Release of Nucleotides from active brain tissue

Pull & McIlwain (1972) showed that adenine nucleotides were released from electrically stimulated brain slices (Fig. 16). They calulated the amounts released per single stimulus (3 - 7 pmole/g) and suggested that a large proportion of the nucleotide material may have been in the form of ATP. Further discussion of these findings is continued below.

Effect of ATP on cerebral blood flow & metabolism

The nature of local control of blood flow in the brain has been a longstanding problem, similar to that in skeletal muscle. In 1890 Roy & Sherrington described an intrinsic control mechanism 'by

which the blood supply of various parts of the brain can be varied locally in accordance with local requirements'. In view of the probable major role that ATP plays in the control of local blood flow in skeletal and cardiac muscle, the effects of ATP, AMP and adenosine on the cerebral vasculature were explored (Forrester, Harper, MacKenzie & Thomson, 1979). Perivascular application of ATP to cat pial arterioles caused dilatation at a threshold concentration of 10^{-11}M. Pull & McIlwain calculated that the total adenine nucleotides released from stimulated brain slices lay between 3 -7 pmole/g for a single stimulus (see above). Assuming that only one tenth of this was ATP and taking the extracellular volume of the brain slice as 0.5 ml/g, a concentration of around 0.3 pmole/0.5 ml, or 6 x 10^{-10}M, can be computed. This value compares favourably with the threshold value of 10^{-11}M causing dilatation when applied perivascularly. It is thus concluded that ATP is released in amounts that are more than adequate to produce maximum local vasodilatation.

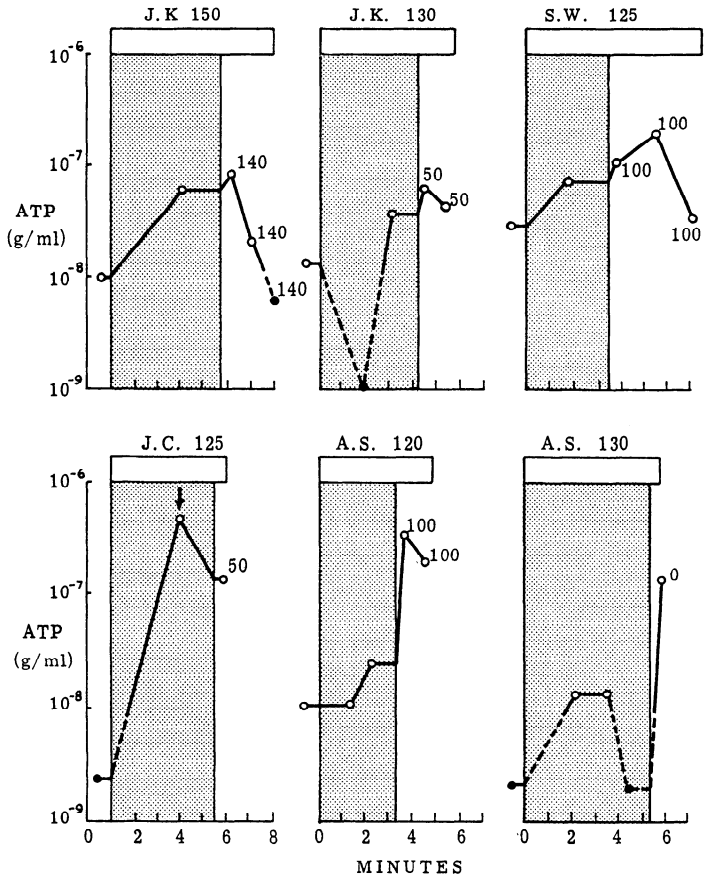


Fig. 11. Concentrations of ATP in venous plasma before, during and after arterial occlusion and exercise. Clear rectangles, duration of exercise; shaded areas, time of arterial occlusion. Resting systolic blood pressure given above each figure. Filled symbols, samples below assay threshold (dashed lines). Vertical arrow in *d*, cuff pressure lowered to obtain sample. Figures above post-occlusion samples indicate cuff pressure when sample was taken. (From Forrester, 1972, *J. Physiol., London*).

Intracarotid administration of ATP produced a surprising result in both cat and baboon (Figs. 17 & 18). In both cases the cerebral blood flow was approximately doubled when ATP was infused into the carotid artery at a rate of 10^{-6} mole/min. Taking into account the carotid blood flow in each case, the calculated threshold concentration in cats was 4 x 10^{-9}M and in baboons 4 x 10^{-8}M. the threshold response to adenosine in the baboon was 4 x 10^{-7}M. No significant effects were seen with AMP, pyrophosphate or inorganic phosphate. An interesting finding was the relationship seen between intravasuclar ATP and the oxygen consumption in the baboon experiments. Table I shows that the oxygen consumption was raised by about one and a half times when 10^{-6}mole/min ATP was infused into the carotid artery of baboon.

TABLE 1. Cerebral blood flow and oxygen consumption during ATP infusions in five baboons. Figures presented are mean ± S.E.M.

		ATP (moles/min, intracarotid)			
	Base line	10^{-9}	10^{-8}	10^{-7}	10^{-6}
CBF (ml./100 g.min)	49 ± 11	66 ± 11	71 ± 13	94 ± 24	116 ± 10
		*$P < 0.05$	$P < 0.01$	$P < 0.05$	$P < 0.001$
$CMRO_2$ (ml.O_2/100 g.min)	2·9 ± 0·3	3·2 ± 0·5	3·4 ± 0·4	4·3 ± 0·7	4·5 ± 0·5
		P = N.S.	P = N.S.	$P < 0.05$	$P < 0.01$

* By Student's paired *t*-test (base line *vs.* ATP infusion). N.S. = not significant.

(Forrester, Harper & MacKenzie, 1975, J. Physiol. London.)

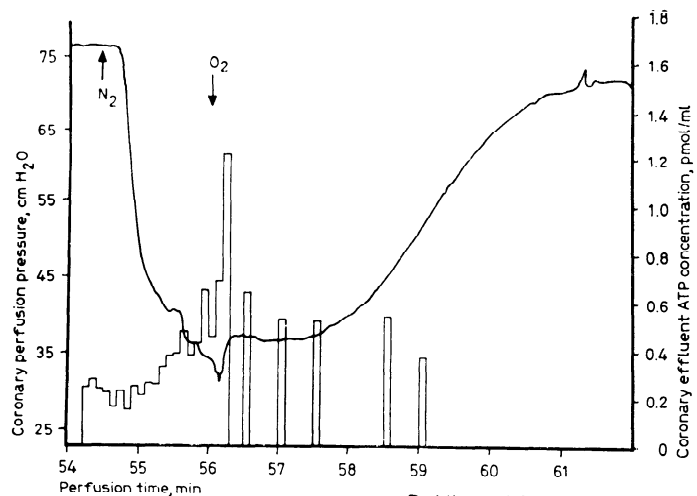


Fig. 12. Effects of a single period of hypoxia on the coronary perfusion pressure and effluent ATP concentration. Flow rate was constant at 4.8 ml/min. Perfusion pressure recorded continuously. Effluent ATP concentrations are average values during 6 sec collection periods. (From Paddle and Burnstock, 1974, *Blood Vessels, S. Karger AG. Basel*).

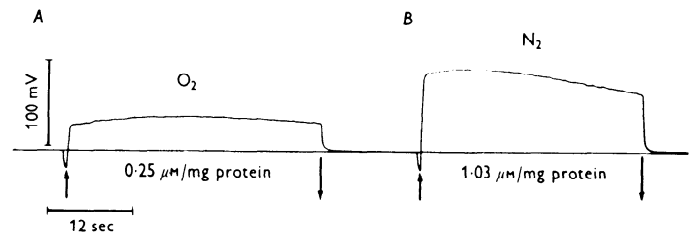


Fig. 13. Emission of light from firefly extract on addition of cells resuspended in either: A, oxygenated or B, nitrogen-equilibrated buffer solution. pH 7.4. Each signal represents amount of ATP extruded after cells had been in contact with respective buffer solutions for 30 sec. at 37°C. (From Forrester and Williams, 1977, *J. Physiol. London*).

Conclusions

It now seems evident that active skeletal muscle, cardiac muscle and brain tissue release significantly high concentrations of ATP into the extracellular space to affect profoundly the local blood flow. A residual amount of ATP and other nucleotides is most likely to reach the general circulation and indeed nucleotides have been detected in the human circulation as long as 5 min after whole body exercise (Parkinson, 1973). The question then arises: can circulating nucleotides and derivatives released from active skeletal muscle achieve levels in the arterial blood sufficient to affect cerebral metabolism? Is there some substance to the adage *'mens sana in corpore sano'?* It remains to be determined what proportion of derivatives, or the nucleotides themselves, can survive passage through the lungs. Some preliminary data in-

dicates that if ATP is infused in high enough quantities into the pulmonary artery of baboon, micromolar levels can be sustained in the arterial circulation without obviously compromising the general circulatory welfare (Evans, Forrester & Mueller, 1978). Other effects of circulating nucleotides are well documented and recently the uptake and supply of purine compounds by the liver has been emphasized (Pritchard, *et al,* 1975). These findings prompt the suggestion that there exists a system of 'metabolic communication' in the body mediated by circulating purine compounds.

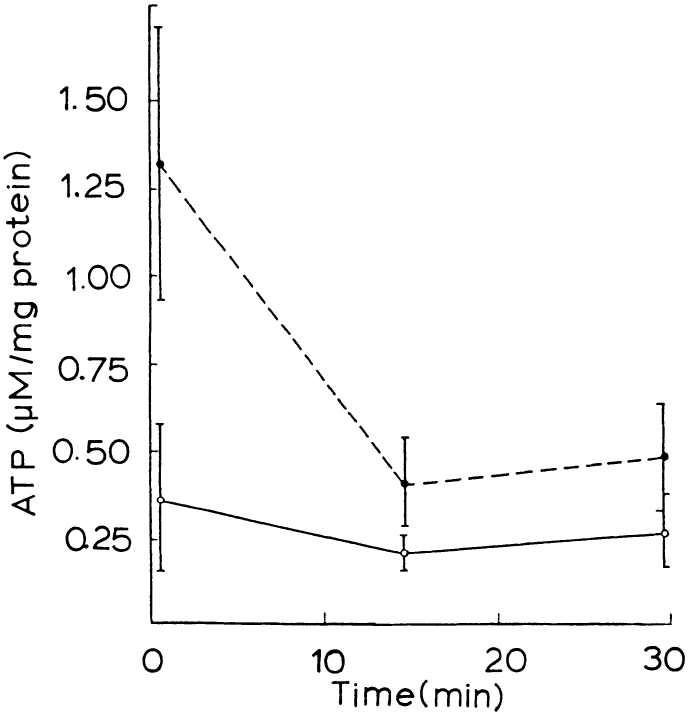


Fig. 14. Summated results from experiment shown in previous figure. Difference between points at 1 min of incubation is highly significant ($0.001 < P < .01$). Each point is average ± S.D. (n=6). (From Forrester and Williams, 1977. *J. Physiol., London).*

Implications for the future

The evidence presented leaves us with an outstading problem that is difficult to interpret within current concepts. How does ATP traverse, or act beyond, the cell membrane?

The clearest evidence of release of ATP from (or through) an excited membrane has been provided by Israel, Lesbats, Meunier & Stinnakre (1976). They have demonstrated very elegantly the release of ATP in response to single nerve impulses applied to the electric organ of *torpedo.* A diagram of the experimental set-up is shown in Fig. 19. The electric organ can be regarded as a gigantic motor end-plate without the underlying skeletal muscle element. It is supplied by a cholinergic motor nerve. Israel *et al* stimulated the motor nerve and recorded the post-synaptic response from the electric organ. At the same time they arranged for the surface of the organ to be perfused with extract of firefly lanterns. Figure 20 shows the response of the superfusing firefly extract to single stimuli applied to the motor nerve. A discrete light signal is recorded for each nerve impulse, even in the case of three nerve stimuli delivered in quick succession. The post-synaptic source of this ATP release was demonstrated by the fact that the light signal became diminished when curare was applied to the synaptic juction *via* the superfusate (Fig. 21). The drug eserine, an anticholinesterase, had the effect of enlarging the light signal, (Fig. 22) indicating that the release of ATP was associated with activation of the acetylcholine receptor and subsequent depolarization of the post-synaptic membrane. This point was resolved neatly by blocking the receptor with curare and then superfusing a high potassium solution to produce depolarization of the post-synaptic membrane. A light signal was produced by this maneuvre, indicating that the ATP release was associated with membrane depolarization rather than with activation of the cholinergic receptor.

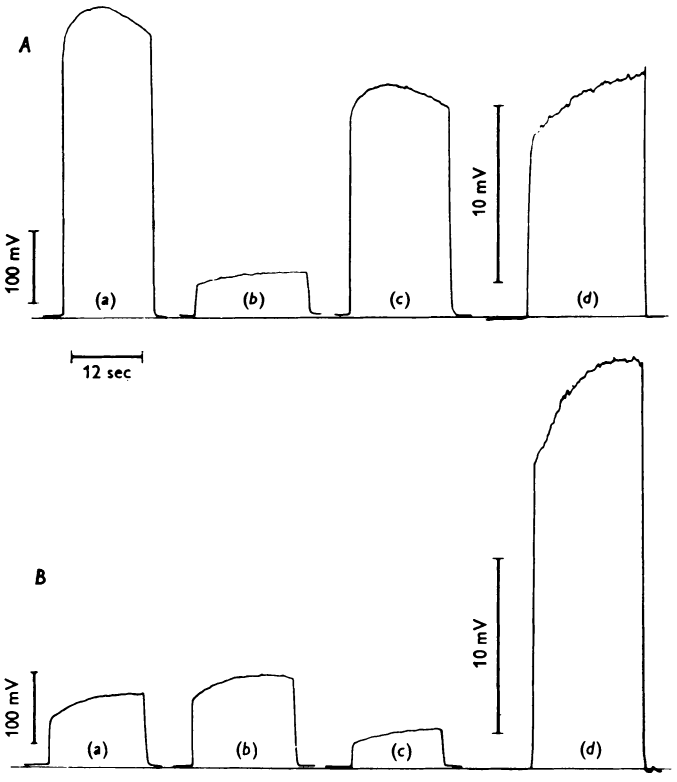


Fig. 15. Emission of light from extract in response to a cell suspension exposed alternately to hypoxic and oxygenated buffer solution. A (a), signal after exposure of cells to hypoxic buffer; (b), response after cells had been returned to oxygenated medium; (c), response when returned to hypoxic buffer; (d), response when finally returned to oxygenated medium; note increase in amplification scale. B, (a) - (d), paired oxygenated controls matching the solutions tested in A. (From Forrester and Williams, 1977, *J. Physio., London*).

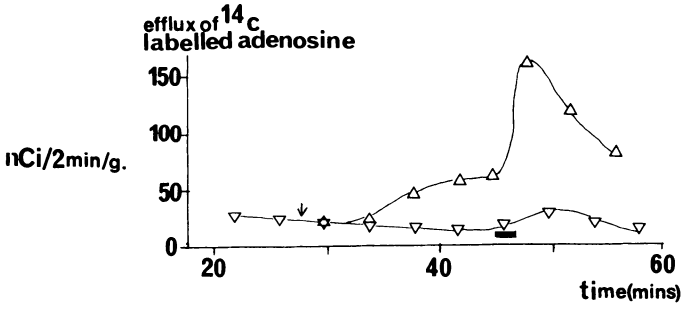


Fig. 16. Effect of stimulating isolated guinea-pig neocortex on output of ^{14}C-labelled derivatives of adenine into media lacking oxygen. The tissue was pre-incubated in oxygenated saline solution containing ^{14}C-adenine. Arrow indicates when hypoxic buffer was applied. Horizontal bar indicates period of stimulation at 32 Hz. for 2 min (▽), oxygenated solution; (△), hypoxic solution. Note that stimulation + hypoxia produce great outflux of label. (From Pull and McIlwain, 1972, *Biochemical Journal*).

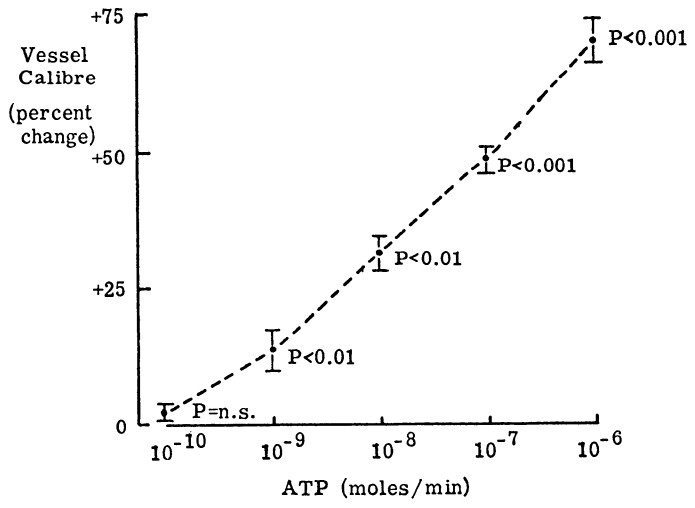


Fig. 17. Effect of intracarotid infusions of ATP on pial arteriolar calibre in 8 cats (Mean ± S.E.). P values obtained by comparing test effect with vessel calibre just prior to infusion. N.S., not significant. (Forrester, Harper, MacKenzie and Thomson, 1979, *J. Physiol. London,* in Press).

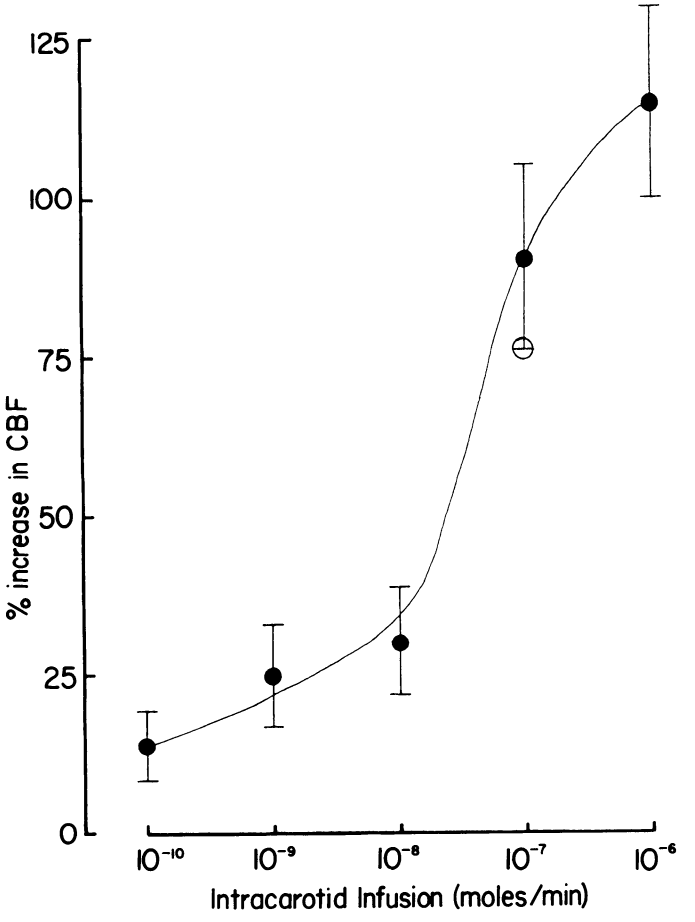


Fig. 18. Increase of baboon blood flow (•) in response to intracarotid ATP infused at 10^{10}-10^{-6} moles/min (Mean ± S.E.). o, response to 10^{-7} moles/min after disruption of the blood-brain barrier. (Forrester, Harper, MacKenzie and Thomson, 1979, *J. Physiol., London,* in Press).

We are left, then, to speculate about the mode of release of ATP from depolarizing membranes. Two possibilities suggest themselves at the present time.

The first can be considered within current concepts of membrane structure and takes into account the protein moieties 'floating' within the lipid bilayer (Singer & Nicolson, 1972). Alteration of protein configuration during depolarization of the membrane may release ATP from certain ATP-Ca-protein complexes in the membrane. The existence of these complexes was proposed by R.J.P. Williams in 1959 and there is now much evidence to support his view. Indeed the action of calcium chelating agents such as EDTA and EGTA on exitable membranes is to increase the levels of ATP in the bathing medium (Koketsu & Miyamoto, 1961; Kuperman, Volpert & Okamoto, 1964; Forrester & Williams, 1977).

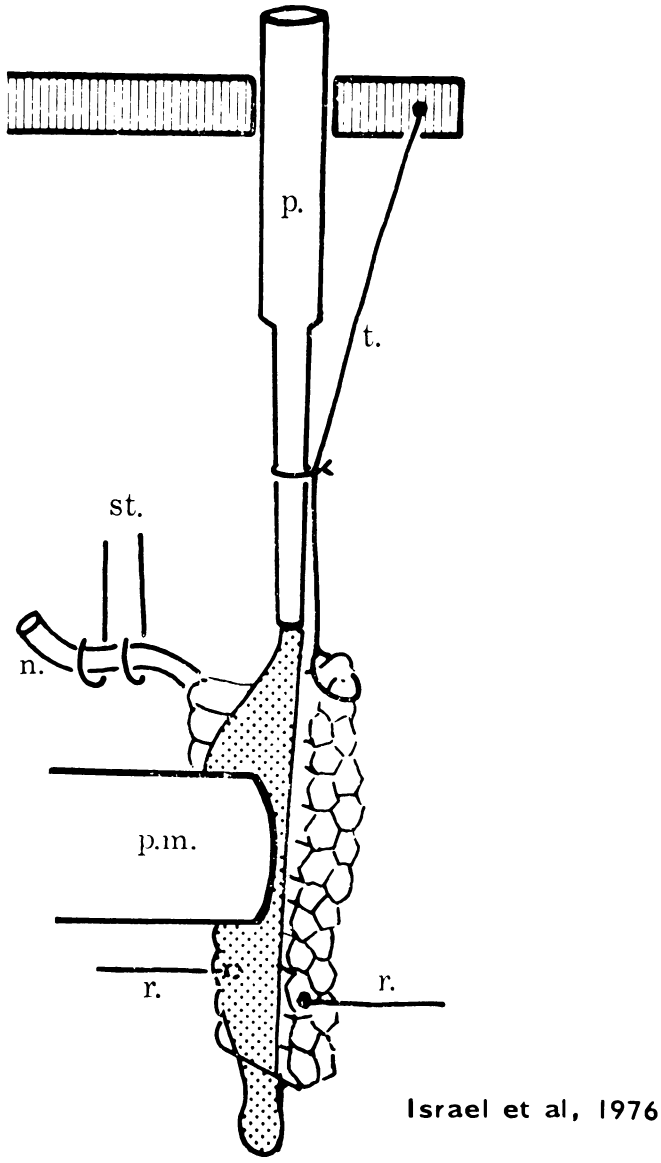
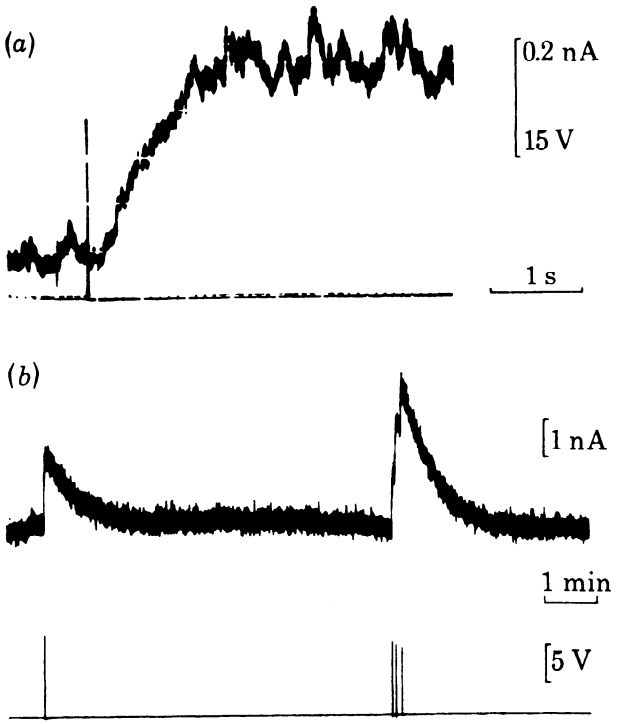
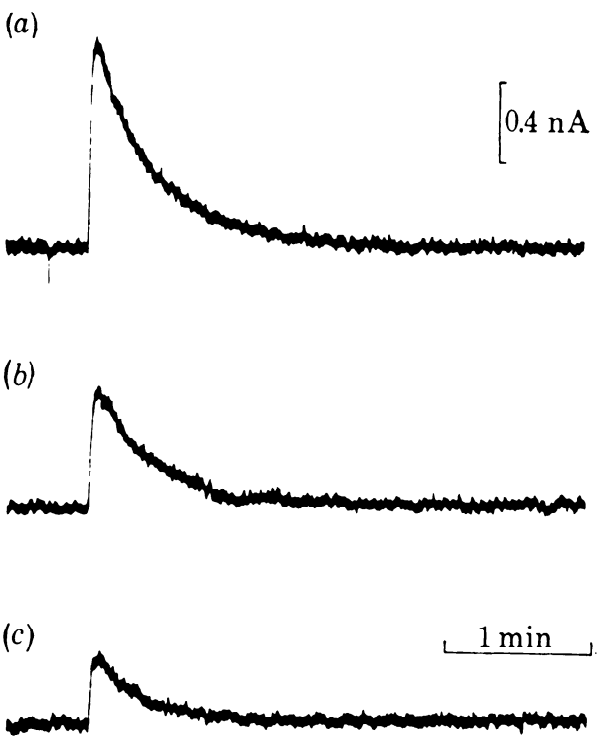


Fig. 19. Experimental set-up to measure post-synaptic release of ATP from electric organ of torpedo. Firefly extract is perfused over the surface of the organ from a pipette (p). Thread (t) stabilizes pipette and tissue. Nerve (n) stimulated through silver-silver chloride electrodes (st). Light signal from firefly recorded by photomultiplier tube (p.m.). Post-synaptic electrical response recorded with platinum electrodes. (From Israel, Lesbats, Meunier and Stinnakre, 1976, *Proc. Roy. Soc. B., London*).



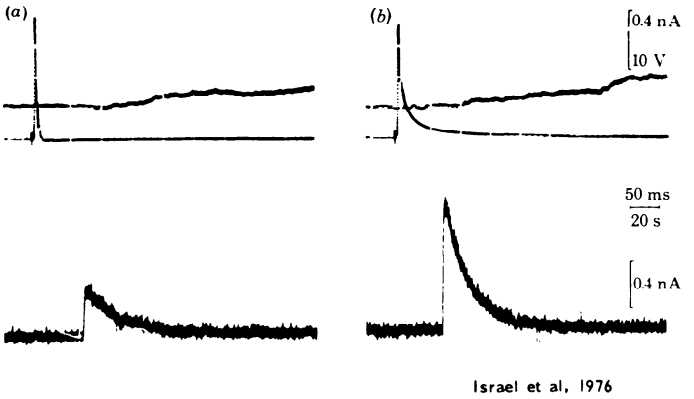
Israel et al, 1976

Fig. 20. Release of ATP after single nerve impulses. (a) lower trace: oscilloscope record of electrical response (post-synaptic) to a single stimulus applied to the nerve; upper trace: intensity of the p.m. current due to light emission resulting from the reaction of ATP with the firefly extract. (b) Responses to single and triple stimulation of the nerve. (Different preparation). Upper trace: light emission; lower trace: electrical responses. Time constant of the light recording system was 110 ms. (From Israel *et al,* 1976).



Israel et al, 1976

Fig. 21. Effect of curare on the release of ATP. (a), control. (b), after about 80 min in 5 x 10^{-4}M curare. (c), concentration of curare increased to 10^{-3}M. Note marked diminution of light signal indicating depression of ATP release post-synaptically. (From Israel *et al,* 1976).



Israel et al, 1976

Fig. 22. Effect of eserine, an anticholinesterase, on ATP release. (a), control. (b), same preparation 15 min after eserine (10^{-4}M). Slow time base on the lower traces shows the augmentation of ATP release in the presence of an anticholinesterase. (From Israel *et al,* 1976).
(Forrester, Harper & MacKenzie, 1975, J. Physiol. London.)

The second possibility requires a radical change of our views concerning the nature of the excitable cell membrane. For many years a group of workers, led by Ling, have maintained that there is simply not enough energy available to run all of the postulated "pumps" in the cell membrane (Minkoff & Damadian, 1973). Ling has proposed an association-induction hypothesis which regards the cell membrane as having a minor role to play in maintaining the intracellulor environment. It is proposed that the physical state of the cell is maintained by protein-ATP complexes occurring at various *cardinal sites* and that the high intracellular potassium and low intracellular sodium levels result from adsorption of these ions to the protein without consuming energy (Ling, 1978).

Elucidation of the ATP release mechanism may advance our understanding of the relationship between a cell and the external environment.

Acknowledgement: It is a pleasure to thank Professor I.A. Boyd, Professor A.R. Lind, Dr. M.O. Hassan, Dr. C.A. Williams, Dr. R.G. Evans and Dr. Hiltrud Mueller for their collaboration and support without which much of this work would not have been possible.

The cerebral blood flow studies were performed at the Wellcome Surgical Research Institute, University of Glasgow in collaboration with Dr. Eric MacKenzie, Dr. Murray Harper and Mr. Euan Thomson. I am grateful to them and the technical Assistance provided.

BIBLIOGRAPHY

Abood, L.G., Koketsu, K. & Miyamoto, S. (1962). Outflux of various phosphates during membrane depolarization of excitable tissues. *Am. J. Physiol.* 202: 469-474.

Afonso, S., Ansfield, T.J., Berndt, T.B. & Rowe, G.C. (1972). Coronary vasodilator responses to hypoxia before and after aminophyllline. *J. Physiol. London.* 221: 589-600.

Berne, R.M (1963). Cardiac nucleotides in hyposia: possible role in regulation of coronary blood flow. *Am. J. Physiol.* 204: 317-322.

Berne, R.M. (1964). Regulation of coronary blood flow. *Physiol. Rev.* 44: 1-29.

Burnstock, G. (1978). An assessment of purinergic nerve involvement in vasodilatation. In: *Mechanisms of Vasodilatation.* Satellite Symposium 27th Int. Congr. Physiol. Sci. Wilrijk. 278-284. (Karger, Basel).

Boyd, I.A. & Forrester, T. (1968). The release of adenosine triphosphate from frog skeletal muscle in vitro. *J. Physiol. London.* 199: 115-135.

Drury, A.N & Szent-Gyorgyi, A. (1929). The physiological activity of adenine compounds with especial reference to their action upon the mammalian heart. *J. Physiol. London.* 68:213-237.

Duff, F., Patterson, G.C. & Shepherd, J.T. (1954). A quantitative study of the response to adenosine triphosphate of the blood vessels of the human hand and forearm. *J. Physiol. London.* 125: 581-589.

Evans, R.G., Forrester, T. & Mueller, H.S. (1978). Intravascular passage of adenosine triphosphate through lung of baboon. *J. Physiol.* 276: 70-71P.

Forrester, T. & Lind, A.R. (1969). Identification of adenosine triphosphate in human plasma and the concentration in the venous effluent of forearm muscles before, during and after sustained contraction. *J. Physiol. London.* 204: 347-364.

Forrester, T. (1972). An estimate of adenosine triphosphate release into the venous effluent from exercising human forearm muscle. *J. Physiol. London.* 224: 611-628.

Forrester, T. & Hassan, M.O. (1973). Appearance of adenosine triphosphate in the perfusate from active frog skeletal muscle. *J. Physiol. London.* 232: 86-88P.

Forrester, T., Harper, A.M. & MacKenzie, E.T. (1975). Effects of intracarotid adenosine triphosphate infusions on cerebral blood flow and metabolism in the anaesthetizod baboon. *J. Physiol. London.* 250: 38-39P.

Forrester, T. & Wiliams, C.A. (1977). Release of adenosine triphosphate from isolated adult heart cells in response to hypoxia. *J. Physiol. London.* 268: 371-390.

Forrester, T., Harper, A.M., MacKenzie, E.T. & Thomson E., (1979). The effect of adenosine triphosphate and some derivatives on cerebral blood flow and metabolism. *J. Physiol. London.* (in Press).

Giles, R.W. & Wilcken, D.E.L. (1977). Reactive hyperaemia in the dog heart: inter-relations between adenosine, ATP, and aminophylline in the effect of indomethacin. *Cardiovascular Res.* 11: 113-121.

Green, H.N. & Stoner, H.B. (1950). In: *Biological Actions of the Adenine Nucleotides.* pp. 65-103. London: H.K. Lewis and Co.

Holton, P. (1959). The liberation of adenosine triphosphate on antidromic stimulation of sensory nerves. *J. Physiol. London.* 145: 494-504.

Israel, M. Lesbats, B., Meunier, F.M. & Stinnakre, J. (1976). Postsynaptic release of adenosine triphosphate induced by single impulse transmitter action. *Proc. R. Soc. B* 193: 461-468.

Koketsu, K. & Miyamoto, S. (1961). Release of calcium-45 from frog nerves during electrical activity. *Nature, London.* 189: 402-403.

Kuperman, A.S., Volpert, W.A. & Okamoto, M. (1946b). Release of adenine nucleotide from nerve axons. *Nature, London.* 204: 1000-1001.

Lind, A.R. & McNicol, G.W. (1967). Local and central circulatory responses to sustained contractions and the effect of free or restricted arterial inflow on postexercise hyperaemia. *J. Physiol. London.* 192: 575-593.

Ling, G.N. (1978). Maintenance of low sodium and high potassium levels in resting muscle cells. *J. Physiol.* 280: 105-124.

Minkoff, L. & Damadian, R. (1973). Caloric catastrophe. *Biophys. J.* 13: 167-178.

Paddle, B.M. & Burnstock, G. (1974). Release of ATP from perfused heart during coronary vasodilitation. *Blood Vessels.* 11: 110-119.

Parkinson, P.I. (1973). The effect of graduated exercise on the concentration of adenine nucleotides in plasma. *J. Physiol. London.* 248: 72-74P.

Pull, I. & McIlwain, H. (1972). Metabolism of ^{14}c-adenine and derivatives by cerebral tissues, superfused and electrically stimulated. *Biochem. J.* 126: 965-973.

Roy, C.S. & Sherrington, C.S. (1890). On the regulation of the blood-supply on the brain. *J. Physiol. London.* 11: 85-108.

Saltin & Rall (1970). *Mol. Pharmacol.* 6: 13-23.

Singer, S.J. & Nicolson, G.L. (1972). The fluid mosaic model of the structure of cell membranes. *Science. N.Y.* 175: 720-731.

Vahouny, G.V., Wei, R., Starkweather, R. & Davis, C. (1970). Preparation of beating heart cells from adult rats. *Science. N.Y.* 167: 1616-1618.

Williams, R.J.P. (1959). Coordination, chelation and catalysis. In: *The Enzymes.* vol. 1, 391-441.

Williams, C.A. (1977). Responses of isolated heart cells to hypoxia. Ph.D. Thesis, St. Louis University.

LEARNING RESOURCE CENTER AT FASEB MEETING IN DALLAS, TEXAS

Marjorie R. Muench
APS Education Office

Computer-assisted instruction models, videocassette programs, and methods and materials in testing and teaching were exhibited at the Learning Resource Center at the Spring Meeting in Dallas. Five Society members representing institutions from across the country presented poster demonstrations, distributed handouts, and showed videocassette and computer programs in the Center, located in the Exhibit Hall Foyer of the Convention Center. The exhibits were shown for two and one-half days, with the participants giving one-hour presentations each morning and afternoon. An APS representative was available to discuss the displays at other times.

The Learning Resource Center was sponsored by the APS Education Committee as a forum for members to exchange information on the teaching of physiology. The participants in the Center submitted abstracts in the Teaching of Physiology category of the call for abstracts.

Two exhibits demonstrated the use of personal computers for self-instruction. Dr. James E. Randall, from Indiana University School of Medicine in Bloomington, presented a simulation of the squid axon spike using the Hodgkin and Huxley equations. Videomonitors showed a graphic display of the computed action potential, providing a rapid means of following changes in physiological conditions. Dr. Harold I. Modell, from the University of Washington, presented a complete independent study program in respiratory physiology, utilizing several integrated media. Students supplement textbooks with question/answer sets which provide three levels of feedback with the use of latent-image materials. In addition, "lab" exercises simulated with a small computer enable the student to set up experiments to test the concepts learned.

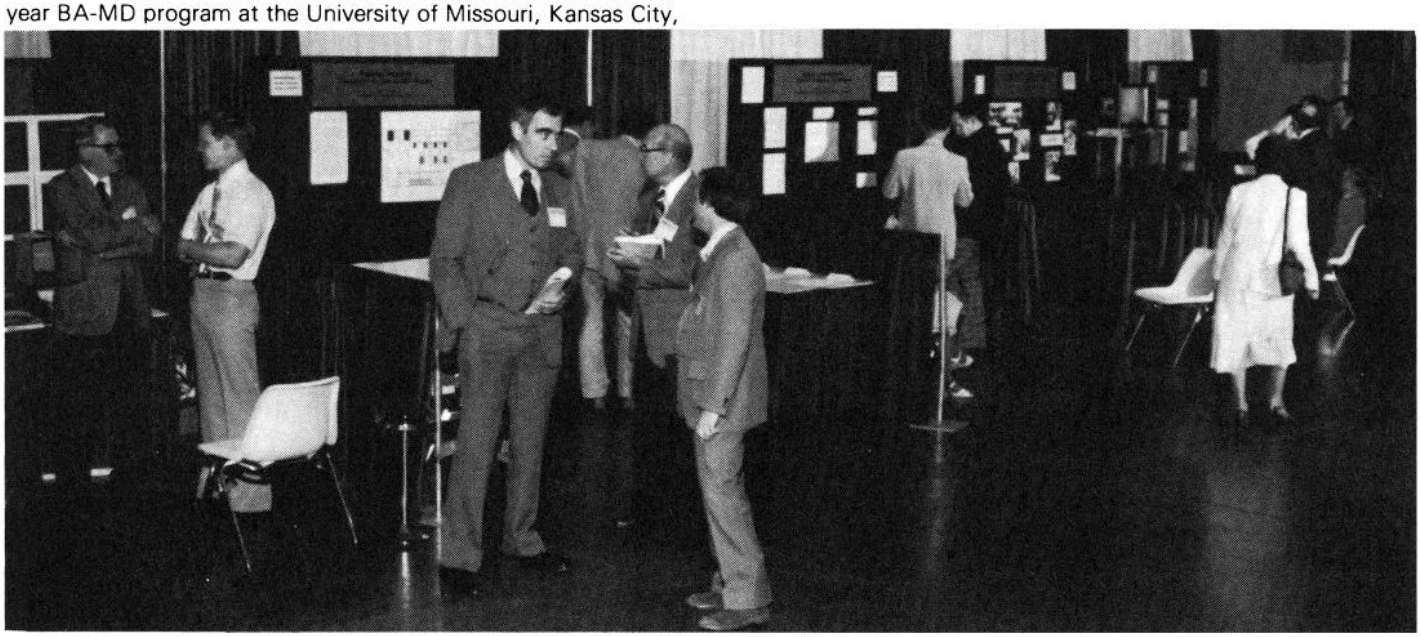
Color videotape programs featuring scanning electron microscopy of the digestive, reproductive, and urinary systems were shown throughout the day. These programs, presented by Dr. Paul C. Harris, are part of a series used to teach functional anatomy at the University of Maine. The scanning electron microscopy sequences enhance gross dissections, slides, and diagrams used in the programs.

The incorporation of physiological instruction throughout a six-year BA-MD program at the University of Missouri, Kansas City, was presented by Dr. John T. Fales. The courses, described on posters and handouts, include college human biology, college medical physiology, clinical and pathophysiology, correlative medicine with advanced physiology, and electives in physiology. The six-year format enables highly-motivated students to study in an accelerated program and to work with medical doctors early in their college education.

Dr. Kermit A. Gaar presented a unique testing and evaluation system used in the teaching of physiology at the Louisiana State University School of Medicine. This is a self-scoring procedure which utilizes a multiple-choice test format. Students select answers to questions by erasing a mark covering symbols on the answer sheet. Symbols are designated correct or incorrect, providing positive feedback to the student and partial credit based on the number of trials to get the correct answer. This test method provides a more accurate assessment of a student's ability and assists in evaluating the relative difficulty of exam questions.

Through the Learning Resource Center, Society members have an opportunity to exchange information on materials and methods in teaching physiology. The participants in the exhibits at Dallas enjoyed sharing their ideas on teaching physiology with their colleagues and other students, and were quite pleased with the response to the exhibits. Over one thousand people visited the exhibits to operate personal computers, watch videotape programs, and discuss the poster demonstrations with the participants. In addition to the presentations submitted by members, the self-instructional slide/tape series developed and produced by the Society's Education Committee were available for viewing.

The educational displays presented in Dallas marked the second exhibition of the Learning Resource Center at a Society meeting. The first Center was held last October at the Fall Meeting in St. Louis, Missouri. Six members participated in the exhibits, displaying computer demonstrations, videocassette programs, and a model of the human brain and spinal column. The Education Committee plans to continue and to expand the Learning Resource Center, with the next exhibits scheduled for the Fall Meeting in New Orleans, Louisiana.



COUNCIL OF ACADEMIC SOCIETIES BRIEF

ASSOCIATION OF AMERICAN MEDICAL COLLEGES • 1 DUPONT CIRCLE NW • WASHINGTON DC
(202) 466-5100 SPRING, 1979 VOL. 4, NO. 3

NATIONAL INSTITUTES OF HEALTH 1980 BUDGET. Although the President and the Administration have repeatedly professed an increasing commitment to biomedical research, the President's FY 1980 budget is an unconvincing reflection of a strengthened commitment. The President's FY 1980 budget request of $3.17 billion for all of NIH, while only slightly below last year's NIH appropriation, would actually mean a 10% reduction in programs due to inflation. In previous years, Congress has always been counted on to appropriate funds for NIH at a level significantly above the President's request, but the pervasive congressional priority to reduce spending may make such optimism unfounded.

In response to the President's budget, Congress has begun the long and complex task of analyzing the budget and developing guidelines for final appropriations. The House and Senate Budget Committees have completed marking up the First Concurrent Budget Resolution which sets nonbinding spending and revenue targets. Both the House and Senate Committees set marks for total discretionary health programs (everything but Medicare and Medicaid) at only about 3% over the President's request. In the fall, the Budget Committees will report a second Concurrent Resolution which will establish binding levels for spending to which the Appropriations Committees must adhere.

Congressional action on the FY 1980 Appropriations bills is proceeding simultaneously with the Budget Committees' deliberations. Both the House and Senate Labor-HEW Appropriations Subcommittees have heard testimony from Administration witnesses and others. The House Labor-HEW Subcommittee expects to mark up the Appropriations bill in mid-May, and the Senate Subcommittee's mark up is expected shortly thereafter. One common theme of the Subcommittee hearings has been how to set priorities for biomedical research if cutbacks in NIH funding are necessary. One of the great concerns this year is the reduction in funds for competing investigator-initiated grants if the budget for NIH is set at or close to the President's request. It is estimated that NIH as a whole could award only 3,062 competing grants in 1980 which would be a reduction from 5,666 in 1979.

Many health interest groups have geared up to defend the NIH budget, stressing the importance of stability in funding for biomedical research. Approximately $250 million would have to be added to the NIH budget to bring it up to the 1979 level in constant dollars. Unlike previous years, groups concerned with NIH funding are asking for stability in the total NIH budget rather than for increases for individual Institutes, and this united front will undoubtedly be more effective.

Another budgetary problem has arisen which is constrained by the President's hold-the-line 1980 budget. In 1978 Congress authorized the first research training stipend increases since 1974. These stipends have fallen far behind in buying power, and NIH Institute directors are determined to increase both pre- and post-doctoral stipends next year. For example, pre-doctoral students would receive $5,040 and post-doctorals (first year), $14,040 annually. The problem is that the Carter budget proposes no increase in the NIH research training budget while about $35 million additional ($181 million total) would be required to meet the cost-of-living increases. If the funds are not added by Congress and stipends are increased, at least 1,500 fewer trainees will be supported in 1980 than 1979.

CLINICAL LABORATORY IMPROVEMENT ACT. On March 9, Senator Javits introduced S.590, the Clinical Laboratory Improvement Act of 1979, which appears to be much more of a laboratory "control" measure than its predecessors. After hearing limited testimony on March 16, the Senate Subcommittee on Health and Scientific Research marked up S.590 on March 21. Although the revised bill is not yet available, it apparently includes some modifications of importance to academic medicine. The marked up version of S.590 was approved by the full Senate Committee on Human Resources on April 11. Companion CLIA legislation has not yet been introduced in the House.

The AAMC has appointed an ad hoc committee which will meet in late April to develop Association policy with regard to this legislation.

COMPENSATION OF HUMAN SUBJECTS FOR RESEARCH INJURIES. DHEW's recent move to require that all human subject consent forms be modified to tell prospective subjects of the availability of compensation for injuries received in the course of experiments, was one of several steps recommended by a 1976 DHEW Task Force. Other steps include requiring that compensation for injuries actually be available from the research institutions. The cost of such compensation would, of course, be paid out of available research funds, thus reducing even more the funds available for biomedical research in general.

A working group has been formed consisting of clinical researchers, insurance industry representatives and AAMC staff to find the least expensive and most workable solution to this very difficult question.

NATIONAL BOARD OF MEDICAL EXAMINERS TRANSFER EVALUATION EXAM. The National Board of Medical Examiners has proposed that its Part I exam no longer be used to evaluate students seeking to transfer into U.S. medical schools. As an alternative, the National Board is exploring the development of a separate examination to be used specifically to evaluate transfer applicants.

The AAMC has recommended that the exam be sufficient in scope and depth to evaluate students' knowledge of the basic sciences and the material contained in courses on the introduction to clinical medicine. It has recommended that there not be a passing score and that scores and percentile ranks in each subject area be reported to the medical schools to be used in evaluating transfer applicants. Other AAMC recommendations are that the exam be made available to any individual and that sponsorship by a medical school or by the AAMC, through the Coordinated Transfer System (COTRANS), not be required.

SAME PLACE, NEW NUMBER. Effective May 21, the AAMC will have a new telephone system. Our new central number will be (202) 828-0400.

The CAS Brief is prepared by the staff of the AAMC Council of Academic Societies and is distributed through the auspices of your member society.

PLEASE POST

ANNOUNCEMENT OF TRAVEL AWARDS

USA NATIONAL COMMITTEE FOR THE INTERNATIONAL UNION OF PHYSIOLOGICAL SCIENCES

The USA National Committee for the International Union of Physiological Sciences (IUPS) is sponsoring a travel grant program to benefit American scientists who could not attend the XXXVIII International Congress of Physiological Sciences in Budapest, HUNGARY, July 13-19, 1980, without such assistance. A limited number of grants will be available. Those eligible to apply for awards are qualified scientists who are citizens or permanent residents of any part of North America, and who plan to participate fully in the Congress. Each applicant will be judged on the merit of his contribution to the Congress in Budapest, considering his training, experience, and potential. Priority will be given to young scientists. Grants will be limited to transportation costs based on the lowest scheduled airline fare from airport of departure and return.

Requests for application forms should be addressed to:

USA National Committee for IUPS
Att: June S. Ewing, Staff Officer
Division of Medical Sciences
National Research Council
2101 Constitution Ave., NW
Washington, DC 20418

Deadline for receipt of completed applications is November 1, 1979. To the degree that it is possible, successful applicants will be notified by December 1, 1979.

PROGRAM

American Physiological Society
Specialty Meeting

"Relation Between Brain Neurotransmitters Endocrine Function"

Michigan State University
Kellogg Center
East Lansing, Michigan

August 22-24
1979

GUEST SOCIETIES: The Endocrine Society and The Neuroscience Society

Members of the Local Committee

Lynn Clemens, Department of Zoology
W.D. Collings, Department of Physiology
Edward Convey, Department of Dairy Science
Richard Dukelow, Endocrine Research Unit
Harold Hafs, Department of Dairy Science
Arthur Kohrman, Department of Human Development
Joseph Meites, Department of Physiology, Chairman
Kenneth Moore, Department of Pharmacology
Raymond Nachreiner, Veterinary Clinic Center
Gail Riegle, Endocrine Research Unit, Department of Physiology
David Rovner, Department of Internal Medicine
Clifford Welsch, Department of Anatomy

Consultants

W.F. Ganong
O.E. Reynolds

Conference Coordinator

Joan Martin Alam, Kellogg Center, (517)-353-7822

SUPPORTING DONORS

We wish to thank the following firms and Michigan State University offices for providing financial support for this meeting:

Mead-Johnson Pharmaceutical Division, Evansville, Indiana.
Eli Lilly Research Laboratories, Indianapolis, Indiana.
American Cyanamid Co., Lederle Laboratories, Pearl River, New York.
McNeil Laboratories, Fort Washington, Pennsylvania.
Hoffman-LaRoche, Inc., Nutley, New Jersey.
Merck, Sharp and Dohme Research Laboratories, Rahway, New Jersey.
The Upjohn Co., Kalamazoo, Michigan.
Ciba-Giegy Corp., Ardsley, New York.
Schering Corp., Bloomfield, New Jersey.
Norwich-Eaton Parmaceuticals, Norwich, New York.
Sandoz, Inc., E. Hanover, New Jersey.
College of Human Medicine, M.S.U.
College of Veterinary Medicine, M.S.U.
The Graduate School, Office of the Dean, M.S.U.
College of Natural Science, M.S.U.
Vice President for Research and Graduate Studies, M.S.U.
College of Osteopathic Medicine, M.S.U.

CONTENTS

ANNOUNCEMENTS

Date and Place of Meeting

The Specialty Meeting of The American Physiological Society will be held in conjunction with The Endocrine Society and The Neuroscience Society, as'Guest Societies' at the Kellogg Center for Continuing Education, at Michigan State University, in East Lansing, Michigan. Scientific sessions will be scheduled from Wednesday afternoon, August 22 through Friday afternoon, August 24. A symposium on "Relation of Brain Amines to Secretion of Pituitary Hormones" will be held on Wednesday P.M. and Friday A.M. While Thursday A.M. and P.M., and Friday P.M. will be devoted to slide and poster sessions.

Registration Desk

Registration, Information and Ticket Sales Desks, and Message Center will be located in the Kellogg Center main lobby.

Registration Hours

Wednesday, August 22 ..... 8 a.m. to 5 p.m.
Thursday, August 23 ..... 8 a.m. to 5 p.m.
Friday, August 24 ..... 8 a.m. to 5 p.m.

Scientist Registration Fees

APS/Endocrine Society/Neuroscience
Society Members $30.00
Nonmembers $50.00
Students $15.00

Student Registration

A certificate or letter signed by the department head, or a student ID card, must be presented by a nonmembr student who registers at the meeting. Those without proper credentials must pay the full nonmember fee.

Advance Registration

To register in advance, mail the registration card with the applicable fee to Specialty Meeting, American Physiological Society, Continuing Education Service, The Kellogg Center for Continuing Education, Michigan State University, East Lansing, Michigan 48824.

Program

The Program will be mailed to advance registrants in July and will be given to current registrants in East Lansing.

Abstract Issue

The June issue of *The Physiologist* contains the program and contributed abstracts submitted for the Specialty Meeting and was mailed in June to all APS members and subscribers. The Endocrine Society and Neuroscience Society members, nonmembers and student registrants will receive their individual copy at the Kellogg Center. Others may purchase the Abstract issue for $1.00. Copies will be available in the lobby of the Kellogg Center. An APS member who does not bring the Abstract issue to the meeting may purchase a replacement copy.

Hotel Reservations

The official registration form is to be used in arranging accommodations for the meeting. Mail the form to Specialty Meeting, American Physiological Society, Continuing Education Service, The Kellogg Center for Continuing Education, Michigan State University, East Lansing, Michigan 48824.

If you must cancel your reservation, or make changes in arrival or departure date, write directly to the Kellogg Center.

Airport Transportation

Taxis are available between the Lansing Capital City Airport and the Kellogg Center on the MSU campus. Taxi fare from the airport to the Kellogg Center is approximately $7.00.

Hospitality

A reception with complimentary buffet, including a cash bar Mixer will be held on Wed. evening, Aug. 22, from 7:30 p.m. -10:00 p.m. in the Big Ten Room of the Kellogg Center. On Thurs., Aug. 23, a banquet will be held at 7:00 p.m.

CONFERENCE INFORMATION

Headquarters for the conference will be The Kellogg Center for Continuing Education on Harrison Road at Michigan Avenue on the campus. It is readily accessible from all expressways via US-127, I-496, or Temporary I-69. Travelers should exit on Trowbridge Road and, as it ends, turn left on Harrison Road to the gated parking lot adjacent to the center. The parking fee is 50 cents upon leaving. Both East Lansing's bus station and the regional Amtrak station are within about a half mile of the center. Taxis serve between the center and the North Central and United Airlines flights at Lansing's Capital City Airport.

Housing at the center may be reserved by completing and returning the Registration. Requests must be made at least two weeks prior to the conference to guarantee housing at the center. A confirmation will be mailed to you, time permitting. If Kellogg Center is filled, a reseration will be made for you at a nearby motel which will confirm the reservation, time permitting. Kellogg Center reservations will not be held past 6 p.m. unless a guarantee or advance payment is made.

Your preference for conference meals should be indicated on the registration form. Reserved meal tickets are held until 15 minutes before serving time and then released for general sale. You should consider your conference reservations confirmed unless you are notified to the contrary.

If you need to be contacted at the Kellogg Center, the telephone is 517/332-6571.

This conference is under the guidance of Joan Martin Alam, Conference Coordinator, Continuing Education Service, The Kellogg Center for Continuing Education, Michigan State University, East Lansing, Michigan 48824.

Telephone 517/353-7822.

COSTS

Registration fees: APS/Endocrine Soc./ Neuroscience Soc.
Members $30.00
Nonmembers $50.00
Students $15.00

Meals: All meals in Big Ten Room
Reception Wed., Aug. 22 ..... Cash bar
Continental Breakfast, Thurs., Aug. 23, 8 AM $1.85
Luncheon, Thurs., Aug. 23 ..... $4.15
Banquet, Thurs., Aug. 23, 7 PM $9.00
Continental Breakfast, Fri., Aug. 24, 8 AM $1.85
Luncheon, Fri., Aug. 24 ..... $4.15

Housing: Half twin-bed room, $12.50 plus 4% tax per night; Single room, $21.00 plus 4% tax per night.

REFUNDS: Prepayment for registration fees and meals will be made automatically upon cancellation by mail or phone before Aug. 21. Later refunds must be approved by the coordinator, Joan Martin Alam.

SCIENTIFIC PROGRAM

WEDNESDAY 1:30 PM AUGUST 22, 1979 -- KELLOGG AUDITORIUM

SYMPOSIUM: INTERACTIONS BETWEEN HYPOTHALAMIC NEUROTRANSMITTERS AND PITUITARY FUNCTION, PART I.

Chairman: J. Meites

1:30 Announcements and Introduction: J. MEITES.

2:00 Aminergic Innervation of the Hypothalamus, C.H. SAWYER, Department of Anatomy, UCLA, Los Angeles, California.

2:30 Endocrine Influences on Aminergic Neuronal Systems in the Hypothalamus, K.E. MOORE, Department of Pharmacology, M.S.U.

3:00 Mechanisms by Which Brain Amines Influences Endocrine Function, F. LABRIE, Medical Research Council, Group in Molecular Endocrinology, Laval University, Quebec City, Canada.

3:30 Pituitary Hormones in the Brain; What is Their Function?, D. KRIEGER, Mt. Sinai Medical Center, New York, N.Y.

4:00 Effects of Hypothalamic Hypophysiotropic Hormones on Behavior, R. MOSS, Department of Physiology, Southwestern Medical School, University of Texas, Dallas, Texas.

4:30 General Discussion.

THURSDAY 9 AM AUGUST 23, 1979 - KELLOGG AUDITORIUM

Session I-PROLACTIN

Co-chairmen: E.M. Convey and C.W. Welsch

9:00 *1.* Evidence for opiate modulation of hypothalamic dopamine and its influence on prolactin synthesis and release. I.S. LOGIN, I. NAGY and R.M. MacLEOD, University of Virginia School of Medicine.

9:15 *2.* Opioid peptide-induced inhibition of the release of dopamine into pituitary stalk blood. G.A. GUDELSKY and J.C. PORTER, University of Texas Southwestern Medical School at Dallas.

9:30 *3.* Role of central neurotransmitters in the action of morphine (M) on the secretion of prolactin (PRL), growth hormone (GH) and thyrotropin (TSH). J.I. KOENIG*, M.A. MAYFIELD* and L. KRULICH, University of Texas Health Science Center at Dallas.

9:45 *4.* Evidence that the central serotoninergic (5-HT) system does not mediate changes in the secretion of prolactin (P) and TSH induced by ether stress in the rat. M.K. STEELE*, R.J. COPPINGS*, M.A. MAYFIELD*, and L. KRULICH, University of Texas Health Science Center at Dallas.

10:00 *5.* Dopa accumulation in median eminence: an index of tuberoinfundibular dopaminergic nerve activity. K.T. DEMAREST* and K.E. MOORE, Michigan State University.

10:15 *6.* Tuberoinfundibular dopaminergic (TI-DA) nerve activity during the estrous cycle of the rat. C.A. JOHNSTON*, K.T. DEMAREST* and K.E. MOORE, (SPON: G.D. RIEGLE) , Michigan State University.

10:30 *7.* Apparent association of dopamine with the prolactin secretory granule. D.D. NANSEL, G.A. GUDELSKY, and J.C. PORTER, University of Texas Southwestern Medical School at Dallas.

10:45 *8.* Effect of amineptine on hypothalamic catecholamine turnover and serum prolactin release in male rats. C.A. HODSON, R.W. STEGER, D.A. VAN VUGT* and J. MEITES, Michigan State University.

11:00 *9.* Plasma prolactin increase induced by electrical stimulation of amygdaloid nucleus. F. VELASCO*, M. VELASCO, H. MUNOZ* and A. PARRA, National Medical Center, IMSS at Mexico City.

11:15 *10.* The effect of substance-P on prolactin content of rat anterior pituitary gland *in vitro.* L. DE PALATIS* and R.P. FIORINDO, The Ohio State University.

11:30 *11.* Mechanisms by which adrenalectomy increases prolactin release. F.C. LEUNG*, H.T. CHEN*, S.J. VERKAIK, R.W. STEGER, G.A CAMPBELL * and J. MEITES, Michigan State University.

11:45 *12.* Characteristics of catecholaminergic neurons in the median eminence (ME) and neurointermediate lobe (NIL) of the rat. R.H. ALPER*, K.T. DEMAREST* and K.E. MOORE, Michigan State Univ.

Note: For all contributed paper sessions the number following the time of presentation is an abstract index number. Asterisk indicates non-member of a participating society.

THURSDAY PM AUGUST 23, 1979 - KELLOGG ROOM 103 A, B

SESSION II—POSTER SESSION I

(Authors will be at their posters from 1PM to 2PM on both Thursday and Friday)

Arrangements: W.D. COLLINGS

Board No.

1 *13.* The Effect of Heat Acclimation on the Hypothalamic Response to Norepinephrine (NE). JOHN V. CHRISTMAN* and CARL V. GISOLFI. Univ. of Iowa, Iowa City.

2 *14.* GABA Modulin: An Endogenous Protein which Controls GABA Receptor Function and Membrane Phosphorylation. A. LEON*, A. GUIDOTTI* and E. COSTA. Lab. Preclin. Pharmacol. NIMH, St. Elizabeth's Hosp., Washington, D.C.

3 *15.* Diurnal Variation in Naloxone Excitation of Dorsal Horn Units in the Spinal Cat. JAMES L. HENRY. Dept. of Research in Anesthesia, McGill Univ., Montreal, P.Q., Canada.

4 *16.* Neurochemical and Behavioral Correlates of Type A and B MAO Inhibtion. V.N. LUINE, V.P. BABCOCK, C. PADEN and B.S. McEWEN. The Rockefeller University, New York, NY.

5 *17.* Comparative Effects of Estrogens, Catechol Estrogens, and Catecholamines on Tyrosine Hydroxylase Activity in Striatal and Hypothalamic Tissue Extracts. MARK M. FOREMAN and JOHN C. PORTER. Dept. OB/GYN & Physiol., Green Ctr. Reprod. Biol. Sci., Southwestern Med. Sch., Dallas, TX.

6 *18.* Uptake of Biogenic Amines by Regional Synaptosomes from Neonatal Sheep Brain: Effect of *In Utero* Thyroidectomy. WALTER B. ESSMAN, J. AYROMLOOI*, and ERIC J. ESSMAN. Queens College, CUNY, Flushing, NY and Long Island Jewish-Hillside Med. Ctr., New Hyde Park, NY.

7 *19.* Characteristics of Tuberoinfundibular (TI) and Nigrostriatal (NS) Dopaminergic Neurons in Aged Male and Female Rats. G.D. RIEGLE, K.T. DEMAREST* and K.E. MOORE. Dept. of Physiol. and Pharmacol., Michigan State Univ., East Lansing.

8 *20.* Adrenocorticotrophic Hormone Effects on ^{14}C-Choline Accumulation by Rat Brain Synaptosomes. J.W. VEALS* AND F.L. STRAND. Schering Corp., Bloomfield, NJ and New York Univ. Dept. of Biol., Washington Square, NY.

9 *21.* Lack of Fast Rate-Sensitive Feedback Suppression of ACTH Secretion by Cortisol in Resting and Stressed Adrenalectomized Dogs. JOHN S. COWAN. Univ. of Ottawa, Ottawa, Canada.

10 *22.* Anti-Progesterone Antiserum Elicits Gonadotropin Secretion Independent of Progesterone Concentration. KERRY L. CHEESMAN* and ROBERT T. CHATTERTON, JR. Depts. of Physiol. and Biophys., and OB/GYN, Univ. of Illinois Med. Ctr., Chicago.

11 *23.* Inhibition by Rat Serum of Prolactin (PRL) Production by Rat Anterior Pituitary Cells *In Vitro*. W.C. HYMER and E.C. AUGUSTINE. The Pennsylvania State University, University Park.

12 *24.* Regional Blood Flow in Ovine Cerebral and Neurohypophyseal Capillary Beds. R.B. PAGE*, R. BRENNAN*, M. HERNANDEZ and D. FUNSCH*. Milton S. Hershey Med. Ctr. of the Pennsylvania State Univ., Hershey.

13 *25.* Pre-Effector Cell Dopaminergic Modulation of Pancreatic Insular Secretions. E. SAMOLS, J. STAGNER* and G. WEIR. VA Med. Ctr. and Dept. of Med., Univ. of Louisville, KY and Univ. of Virginia, Richmond.

2:30 *28.* Role of serotonin in LH secretion. R.F.WALKER* and P.S. TIMIRAS, University of California at Berkeley.

2:45 *29.* Positive and negative feedback effects of ovarian steroids on LH release in ovariectomized rats following midbrain transection of the ascending noradrenergic pathway (ANP). D.K. CLIFTON* and C.H. SAWYER, University of California at Los Angeles.

3:00 *30.* Effects of morphine and naloxone on the phasic release of gonadotropins. P.W. SYLVESTER*, H.T. CHEN* and J. MEITES, Michigan State University.

3:15 *31.* Catecholamine synthesis enzyme activity during the estrus cycle. L.A. CARR and J.L. VOOGT, University of Louisville and University of Kansas Medical Center.

3:30 *32.* Hypothalamic tyrosine hydroxylase activity and plasma prolactin and luteinizing hormone levels in the developing rat. P.J. MURPHY* and A.E. JIMENEZ*, (SPON: D.C. MEYER), University of Louisville.

3:45 *33.* Effects of gonadal hormones on cholinergic activity in discrete brain nuclei. W.R. CROWLEY, E.A. MUTH* and D.M. JACOBOWITZ, University of Tennessee.

4:00 *34.* Effect of bromocriptine treatment on plasma LH concentrations in ovariectomized ewes. T.G. HILL*, C.W. ALLISTON and P.V. MALVEN, Purdue University.

4:15 *35.* Fluctuation of acetylcholine concentration in blood during estrous cycle. N. HAGINO, A. MODAK and W.B. STAVINOHA, University of Texas Health Science Center at San Antonio.

4:30 *36.* Hypothalamic vs. gonadal mechanisms for depression of pituitary LH release during starvation. G.A. CAMPBELL*, T. IEIRI*, R.W. STEGER, H.T. CHEN* and J. MEITES, Michigan State University.

4:45 *37.* Compensatory gonadal hypertrophy assay in rats. T. BECK*, D. MILLS and W.R. GOMES, The Ohio State University.

THURSDAY 2:00 PM AUGUST 23, 1979-KELLOGG AUDITORIUM
SESSION III — GONADOTROPINS
Co-Chairmen: D. Rovner and R. Nachreiner

2:00 *26.* Progesterone-induced temporal alterations in LHRH concentrations in several brain nuclei: effects of NE synthesis inhibitor, diethyldithiocarbamate (DDC). J.W. SIMPKINS*, P.S. KALRA* and S.P. KALRA, University of Florida.

2:15 *27.* Pulsatile LH patterns in ovariectomized (OVX) rats: involvement of norepinephrine and dopamine in the release of LHRH and LH. A. NEGRO—VILAR, J.P. ADVIS*, S.R. OJEDA and S.M. McCANN, University of Texas Health Science Center at Dallas.

FRIDAY 9:00 AM AUGUST 24, 1979 -- KELLOGG AUDITORIUM
SYMPOSIUM: INTERACTIONS BETWEEN HYPOTHALAMIC NEUROTRANSMITTERS AND PITUITARY FUNCTION, PART II.
Co-Chairmen: G. Riegle and R. Dukelow

9:00 Regulation of LH and FSH Secretion in Rats and Primates, J. PORTER, Dept. of Obstet/Gynecol, University of Texas Health Sciences Center, Dallas, Texas.

9:30 Dopamine, PIF and Other Regulators of Prolactin Secretion, J. CLEMENS, Eli Lilly Research Labs., Indianapolis, Indiana.

10:00 Regulation of TSH and GH Secretion, J. MARTIN, Massachusetts General Hopital, Boston, Massachusetts.

10:30 Regulation of ACTH Secretion, W.F. GANONG, San Francisco Medical Center, University of California at San Francisco, CA.

11:00 Regulation of MSH Secretion, A. KASTIN, Tulane University Medical School, New Orleans, Louisiana.

11:30 General Discussion.

FRIDAY 1 PM to 2 PM AUGUST 24, 1979 - KELLOGG ROOM 103A,B
SESSION IV—POSTER SESSION II
SEE POSTER SESSION I FOR LOCATION AND TITLE OF POSTERS

FRIDAY 2:00 PM AUGUST 24, 1979 - KELLOGG AUDITORIUM
SESSION PM V—GROWTH HORMONE, PROLACTIN, ADH
Co-Chairmen: L. Clemens and A. Kohrman

2:00 *38.* Stimulation of bioassayable growth hormone secretion by thyrotropin releasing hormone. R.E. GRINDELAND, S.H. YANG*. S.E. OSBORNE*, and T.N. FAST*, NASA-Ames Research Center.

2:15 *39.* On the hypothalamic mechanism by which prostaglandin E_2 stimulates growth hormone (GH) release: *in vivo* and *in vitro* studies. S.R. OJEDA, A. NEGRO-VILAR and S.M. McCANN, University of Texa Health Science Center at Dallas.

2:30 *40.* Amitriptyline-induced suppresion of growth hormone in acromegaly. A.R. GLASS, M. SCHAAF, and R.C. DIMOND, Walter Reed Army Medical Center.

2:45 *41.* Inhibition of stimulus-secretion coupling in rat lactotroph cells by D-600, manganese, removal of extracellular calcium and dopamine. M.O. THORNER, J.T. HACKETT, K. DANIEL* and M. CALLAHAN*, University of Virginia School of Medicine.

3:00 *42.* Temporal effects of TRH and serotonin (5-HT) on size heterogeneity of plasma prolactin in ovariectomized, polyestradiol phosphate-treated (OVX+PEP) rats. D.M. LAWSON, Wayne State University.

3:15 *43.* Monoamine oxidase activity and serotonin metabolism in the mouse brain. T.R. HALL* and H.R. FIGUEROA*, (SPON. E.A. STEIN), Marquette University.

3:30 *44.* Direct effects of dexamethasone on mammary tumor growth, C.F. AYLSWORTH*, P.W. SYLVESTER*, G.A. CAMPBELL* and J. MEITES, Michigan State University.

3:45 *45.* Melatonin inhibits the *in vivo* pituitary response to LH-releasing hormone in neonatal rats. J.E. MARTIN and S. McKELLAR*, Washington University Medical School at St. Louis.

4:00 *46.* Disassociation of LH and FSH regulation in transition period between regular cycles and constant estrus in old female rats. R.W. STEGER, H.H. HUANG* and J. MEITES, Michigan State University.

4:15 *47.* Hypothalamic norepinephrine and dopamine turnover in ovariectomized old rats treated with gonadal steroid. H.H. HUANG*, J.W. SIMPKINS and J. MEITES, Michigan State University.

4:30 *48.* Diuretic action of clonidine in the rat. M. MILLER, Veterans Administration Medical Center and State Univ. of New York. Upstate Med. Ctr., Syracuse.

4:45 *49.* L-dopa suppresses plasma vasopressin concentration during inhibition of extracerebral dopa-decarboxylse. M.L. BLAIR, I.A. REID, L.C. KEIL and W.F. GANONG, University of California at San Francisco.

ABSTRACTS

CHARACTERISTICS OF CATECHOLAMINERGIC NEURONS IN THE MEDIAN EMINENCE (ME) AND NEUROINTERMEDIATE LOBE (NIL) OF THE RAT. R.H. Alper*, K.T. Demarest* and K.E. Moore, Department of Pharmacology and Toxicology, Mich. State Univ., E. Lansing, MI 48824.

Tuberoinfundibular (TI) and tuberohypophyseal (TH) dopamine (DA) nerves originate in the arcuate nucleus and terminate in the ME and NIL, respectively. The concentrations (ng/mg protein) of DA and norepinephrine (NE), estimated using a radioenzymatic assay, are approximately 110 DA and 40 NE in ME but only 7 DA and 2 NE in NIL. Superior cervical ganglionectomy failed to alter the DA concentration in either brain region, but reduced the NE concentration in NIL. This suggests that DA in ME and NIL is contained in nerves of central origin (TI and TH neuronal systems, respectively), whereas part of the NE in NIL is contained in peripheral NE neurons. The rate of decline of DA and NE following the administration of α-methyltyrosine was used to estimate turnover of these amines in ME and NIL. In both regions the rate of turnover of DA was much greater than that of NE. The accumulation of DOPA 30 min after the administration of 3-hydroxybenzylhydrazine (100 mg/kg) was also used to estimate DA turnover. Three daily doses of estradiol benzoate (25 μg/kg, s.c.) increased DOPA accumulation in ME but not in NIL, whereas 48 hrs of water deprivation increased DOPA accumulation only in NIL. These results indicate that TI and TH DA nerves are regulated by different mechanisms. (Supported by USPHS grant NS 09174, Fellowship NS 06026 and Training Grant GM 07392.)

DIRECT EFFECTS OF DEXAMETHASONE ON MAMMARY TUMOR GROWTH. C.F. Aylsworth*, P.W. Sylvester*, G.A. Campbell* and J. Meites, Dept. of Physiology, Mich. State Univ., East Lansing, MI 48824.

Female Sprague Dawley rats with established DMBA-induced mammary tumors were given daily injections of dexamethasone (DEX) (40 μg/rat), haloperidol (HAL) (0.5 mg/kg) DEX and HALO or 0.85% NaCl, sc for 3 wks. Effects of treatments on mammary tumor diameters were measured. Blood was sampled at weekly intervals in the morning 1 hr following injections. Rats injected with HALO alone showed increased mammary tumor growth and elevated serum prolactin (PRL) levels when compared to control rats. When DEX was injected alone, a significant regression of mammary tumors and reduced serum PRL levels resulted. Simultaneous injections of DEX and HALO caused a significant regression of mammary tumors and elevated serum PRL levels. These results suggest that DEX, a synthetic glucocorticoid, can directly inhibit mammary tumor growth in the presence of elevated serum PRL levels. These results may help explain the regression of mammary tumor growth during postpartum lactation in rats when PRL and corticosterone levels both are elevated due to the suckling stimulus (aided in part by NIH research grants CA10771 from the National Cancer Institute and AM04784 from the National Institute for Arthritis, Metabolism and Digestive Diseases).

COMPENSATORY GONADAL HYPERTROPHY ASSAY IN RATS. Tom Beck*, Douglas Mills and W. R. Gomes. Department of Dairy Science, The Ohio State University, Columbus, Ohio 43210

Two experiments were performed to establish the age, sex, and duration of hemicastration optimum for assay of gonadal hypertrophy. The first experiment tested age and sex. Groups of four male and four female rats were hemicastrated at 25, 30, 35 and 40 days of age (first gonad weight) and sacrificed three days later (second gonad weight). Compensatory hypertrophy considered positive if the slope of the line between the first and second gonad weight was greater than that for first gonad weight over time. Testicular weight increased with age but no testicular hypertrophy occurred. Ovarian weight increased with age and compensatory ovarian hypertrophy (COH) occurred at all ages. The greatest COH occurred when 35 day old females were hemicastrated. The second experiment tested optimum duration of hemicastration. Five groups of four female rats were hemicastrated at 33 days of age. One test group was sacrificed daily for the next five days. One control group, of the same age, was sacrificed with each hemicastrated group. The COH increased linearly over the five days tested. Correction for body weight removed the effect of age. The regression coefficient for ovarian hypertrophy corrected for body weight was 2.50 mg per day hemicastrated. The regression coefficient for the control rats was 0.05 mg per day of age. We found the sex, age and duration of hemicastration which optimized compensatory hypertrophy to be female rats 33 to 38 days of age hemicastrated 5 days.

L-DOPA SUPPRESSES PLASMA VASOPRESSIN CONCENTRATION DURING INHIBITION OF EXTRACEREBRAL DOPA-DECARBOXYLASE. M.L.Blair, I.A. Reid, L.C.Keil and W.F.Ganong. Dept. of Physiology, Univ. of California, San Francisco, CA 94143

When extracerebral dopa-decarboxylase is inhibited by carbidopa (MK486), an agent which does not cross the blood-brain barrier, i.v. L-dopa decreases blood pressure and plasma renin activity (PRA) (JPET 202:209,1977). These effects are often accompanied by increased urine flow, suggesting that vasopressin (AVP) secretion is also decreased. Pentobarbital-anesthetized dogs with renal perfusion pressure held constant received L-dopa (20 mg/kg i.v.) 35 min after administration of carbidopa (20 mg/kg i.v.). AVP decreased from 8.1±1.1 control to 4.9±1.3 pg/ml* 15 min after L-dopa infusion, and was still suppressed to 5.1±1.4 pg/ml* after one hr (n=7). Mean arterial pressure decreased by 52±6 mm Hg*, and PRA decreased to 62±11% of control*. The following data demonstrate that the decrease in AVP after L-dopa is not dependent upon decreased PRA. In 6 dogs pretreated with phenoxybenzamine and propranolol, AVP decreased from 11.5±3.2 control to 5.8±1.7 pg/ml* 15 min after L-dopa infusion and remained suppressed for one hr while PRA did not change. Similarly, L-dopa decreased AVP from 7.8±2.6 to 3.5±1.6 pg/ml* but did not suppress PRA after bilateral renal denervation (n=6). Thus L-dopa suppresses AVP in carbidopa-treated dogs, probably by a direct CNS effect. (*p<.01) (Supported by USPHS grants NS00045 and AM06704 and the Skaggs Foundation.)

HYPOTHALAMIC VS. GONADAL MECHANISMS FOR DEPRESSION OF PITUITARY LH RELEASE DURING STARVATION, G.A. Campbell*, T. Ieiri*, R.W. Steger, H.T. Chen* and J. Meites, Physiology Dept., Michigan State University, East Lansing, MI 48824.

The mechanisms for the depression of hypophysial functions that occur with nutritional deficiencies and starvation have not been fully elucidated. We previously reported that acute starvation caused a reduction in serum LH and FSH in adult male rats, but chronic starvation permitted FSH to return to normal levels. We have since observed that gonadal steroids have a greater LH-depressing potency in starved than in well-fed gonadectomized rats, suggesting that underfeeding results in a lowered 'set point' for hypothalamic regulation of gonadal function. Srebnik et al. (1977) reported that during protein deficiency, gonadal steroid dysgenesis preceded the decline in gonadotropins, and suggested that the fall in circulating steroids may evoke changes in hypothalamic sensitivity. We examined hypothalamic, pituitary and gonadal function during 6 days of total starvation. Serum LH and testosterone each declined steadily throughout this period, and significant depressions in both became evident at about the same time. Serum FSH showed only a moderate decline. By the 4th day, a significant reduction in serotonin (5-HT) content in the anterior hypothalamus appeared. These results suggest that the fall in gonadal steroids during total starvation is caused by a reduction in LH release, not the reverse, and the primary cause may be enhanced release of 5-HT from nerve terminals in the anterior hypothalamus. (Aided by NIH research grant AM04784).

CATECHOLAMINE SYNTHESIS ENZYME ACTIVITY DURING THE ESTRUS CYCLE. L.A. Carr and J.L. Voogt. University of Louisville, Louisville, KY 40232 and University of Kansas Medical Center, Kansas City, KS 66103.

Several studies suggest that hypothalamic catecholamine neurons are involved in regulating the release of luteinizing hormone (LH) and prolactin during the estrus cycle. Cycling female rats were sacrificed at two-hour intervals between 1000 and 1600 hrs on proestrus, estrus and diestrus II. The plasma concentrations of LH and prolactin at the time of sacrifice were determined. The medial basal hypothalamus was assayed for activity of tyrosine hydroxylase and dopamine-β-hydroxylase (DβH). The plasma prolactin concentration increased significantly at 1400 and 1600 hrs on proestrus whereas the proestrus surge of LH was more pronounced at 1600 than at 1400 hrs. There were no significant changes in either hormone at the times measured on the other two days. Tyrosine hydroxylase activity was significantly decreased at 1200 hrs, when compared with other times during proestrus. Although DβH activity was elevated at 1200 hrs on proestrus, it was significantly different from activity at 1600 hrs only. A similar increase occurred at 1400 hrs on diestrus II. No significant changes in either enzyme were observed in the remainder of the hypothalamus. These results suggest a correlation between the activity of catecholamine neurons and release of LH and prolactin although it is not known whether the relationship is a trophic function or a reflection of hormonal feedback. (Supported by NIH Grant HD 11922).

ANTI-PROGESTERONE ANTISERUM ELICITS GONADOTROPIN SECRETION INDEPENDENT OF PROGESTERONE CONCENTRATION. Kerry L. Cheesman* and Robert T. Chatterton, Jr., Departments of Physiology and Biophysics and of Obstetrics and Gynecology, University of Illinois at the Medical Center, Chicago, Illinois 60612

Anti-progesterone antiserum (APA) has previously been shown to be abortifacient in pregnant rats at midgestation, and this action has been assumed to be due solely to changes in progesterone (P) concentrations. Gonadotropins and steroid feedback have not been considered. Highly specific APA was raised in rabbits and purified by DEAE-cellulose chromatography. Final concentration was 20 mg protein/ml with a binding capacity of 6 μg P/ml. Pseudopregnancy was induced in young Sprague-Dawley rats, and 1 ml of (1) APA, (2) APA saturated with P, or (3) P alone (2 mg/ml) was injected i.p. on day 5. Blood samples were drawn every 6 hours by jugular venipuncture. APA treatment resulted in a rapid increase in serum luteinizing hormone (LH), peaking at 12-18 hours before slowly declining. Saturated APA elicited the same response, whereas P alone showed no increase beyond that of oil or NRS controls. Although direct interactions between the antiserum and cellular mechanisms in the anterior pituitary or hypothalamus have not yet been demonstrated, it appears that the APA is capable of stimulating a gonadotropin response independent of serum P concentrations. This increase in LH may be responsible, at least in part, for the abortifacient actions seen. (Supported by PARFR subcontracts P-10 and 102-N of AID/csd-3608).

THE EFFECT OF HEAT ACCLIMATION ON THE HYPOTHALAMIC RESPONSE TO NOREPINEPHRINE (NE). John V. Christman* and Carl V. Gisolfi, Univ. of Iowa, Iowa City, IA 52242

Guide tubes (23 gauge) for intracranial microinjections were stereotaxically implanted above the anterior hypothalamus (AH) of 10 male Sprague-Dawley rats (280-295 g). The animals ran daily at 21.5 m/min for 3 weeks, 5 at 22°C (controls, C), and 5 at 35°C (heat acclimation, HA). Wind velocity was 85 m/min. Initially, daily training duration for both groups was determined by the time required for Tc to rise in the heated rats to 40.4°C. By the end of the first week and for the next 2 weeks Tc was allowed to rise to 41.4°C. Before and after this 3 week period, microinjections of NE (10 μg/μl, delivered bilaterally in 0.5μl) were made at rest and just prior to treadmill exercise at 21.5 m/min. Mean maximal Tc reductions ± S.D. (°C) pre- and post-acclimation, and the ANOVA probabilities (P) of a Control-Heat Acclimation group difference due solely to heat exposure were:

	Resting			Exercising		
Group	Pre	Post	P	Pre	Post	P
C	1.3±.7	1.3±.7		1.0±.4	1.2±.7	
HA	1.2±.2	2.2±.3	.98	.9±.8	1.5±.5	.42

The larger reductions in Tc with heat exposure were usually associated with faster and/or larger increases in Ts. These results suggest that heat acclimation increases the post-synaptic sensitivity and reactivity of the anterior hypothalamic heat-loss pathway to NE.
(Supported by ONR Contract N00014-75-C-0597)

POSITIVE AND NEGATIVE FEEDBACK EFFECTS OF OVARIAN STEROIDS ON LH RELEASE IN OVARIECTOMIZED RATS FOLLOWING MIDBRAIN TRANSECTION OF THE ASCENDING NORADRENERGIC PATHWAY (ANP). D.K. Clifton* and C.H. Sawyer. Dept. Anat., UCLA, L.A., Ca. 90024.

Long term (>5 weeks) ovariectomized rats with midbrain transections which either cut the ANP (experimentals, EX) or terminated just dorsal to it (shams, SH) were treated with ovarian steroids and the resulting changes in LH release were measured. There were no significant differences in LH levels between SH (n=8-9) and EX (n=7-8) rats at 0, 6, or 12 h following the administration of extradiol benzoate (EB; 5ug, sc); however, at 24 and 48 h there was a much greater supression of serum LH in EX animals than in SH rats ($P<0.05$). In contrast, the output of the pituitary in response to LHRH (7ng/100g, iv) was essentially the same in both groups at either 0 or 48 h after EB. We have previously demonstrated that progesterone (P) induces an LH surge in ANP transected ovariectomized rats that are primed 48 h earlier with EB. To see if this surge is dependent on residual noradrenergic neurotransmission, phenoxybenzamine (PBZ; 20mg/kg, ip) was injected at the same time as P (2mg, sc) 48 h after EB (5ug, sc). Although PBZ completely supressed the surge in 6 of 8 SH rats, LH release was not blocked in any of the EX animals (n=8). These results further support the concept that noradrenergic control of LH release is modulatory rather than mandatory.

LACK OF FAST RATE-SENSITIVE FEEDBACK SUPPRESSION OF ACTH SECRETION BY CORTISOL IN RESTING AND STRESSED ADRENALECTOMIZED DOGS. John S. Cowan, Univ. of Ottawa, Ottawa, Can. K1N 9A9

Low stepwise infusions of cortisol in resting adrenalectomized dogs (plateaux $<6\mu g/dl$) were shown to reduce ACTH secretion, but with no effect for 20 min, and maximal steady effect within 1 hr (Cowan & Windle, Endocrinology 103:1173, 1978). In the present study, large, steep-sloped cortisol signals were used to try to evoke faster feedback. 16 expts on 9 adrex male mongrel dogs involved 11 at rest and 5 with dogs stressed by variable infusion of insulin to maintain plasma glucose at 15-40mg/dl. Dogs were maintained on exogenous steroids till 48 hr before the expt. All experiments were carried out under light pentobarbital anesthesia. After a 50 min control period, a 30 min feedback period was initiated by one of two i.v. cortisol signals:(a) injection of 0.3 mg/kg or (b) infusion of 0.046 mg/kg·min.Both raised plasma cortisol above normal physiological limits (within 2 & 6 min resp). In each expt 23 timed venous blood samples were assayed for plasma ACTH (adrenal cell bioassay) and cortisol (fluorimetry). ACTH secretion rates were calculated continuously using a validated single-compartment method. In the unstressed dogs, control period ACTH secretion rates of 0.37-1.68 mU/kg·min showed no significant decline due to the feedback signal until 16-30+ min after its application.In the stressed dogs the comparable values are 0.82-6.24 mU/kg·min and 22-30+ min.Thus at rest or in stress, these large cortisol signals evoked no more evidence of fast, rate-sensitive feedback than did very small signals.(Supported by MRC of Can.)

EFFECTS OF GONADAL HORMONES ON CHOLINERGIC ACTIVITY IN DISCRETE BRAIN NUCLEI. W.R. Crowley, E.A. Muth*, and D.M. Jacobowitz. Univ. of Tennessee, Memphis, TN 38163 and NIMH, Bethesda, MD 20014.

The concentrations of acetylcholine (ACh) and the activity of choline acetyltransferase (ChAT) were measured in microdissected brain nuclei and correlated with plasma levels of luteinizing hormone (LH) in gonadectomized male and female rats given steroid hormone treatment. Castration of males elevated plasma LH and also increased ACh level and ChAT activity in the medial preoptic nucleus, increased ChAT activity in the posteromedial amygdala and elevated ACh levels in the nucleus tractus diagonalis and ventral tegmental area. These changes were partially blocked by daily treatment with testosterone. Testosterone also depressed ChAT activity in the nucleus tractus diagonalis. Treatment of ovariectomized females with estradiol lowered plasma LH but did not affect cholinergic parameters. However, the induction of LH surges produced by administration of progesterone 48 hours after estrogen priming was associated with a decrease in ACh level and ChAT activity in the periventricular nucleus. ChAT activity and ACh levels were also decreased by such treatment in the nucleus tractus diagonalis and ventral tegmentum, respectively. ChAT activity was elevated in the supraoptic nucleus after estrogen plus progesterone. These results suggest that cholinergic neurons in several discrete brain regions may be involved in the feedback effects of gonadal hormones.

DOPA ACCUMULATION IN MEDIAN EMINENCE: AN INDEX OF TUBERO-INFUNDIBULAR DOPAMINERGIC NERVE ACTIVITY. K.T. Demarest* and K.E. Moore. Dept. of Pharmacology and Toxicology, Michigan State University, East Lansing, MI 48824.

Changes in the rate of accumulation of DOPA in the striatum (ST) following the administration of a decarboxylase inhibitor have been used to estimate changes in the activity of nigrostriatal dopamine (DA) nerves. The development of a radioenzymatic assay for DOPA has now permitted the use of this technique to estimate the activity of tuberoinfundibular DA nerves which terminate in the median eminence (ME). In the present studies the concentrations of DOPA in ME and ST were determined 30 min after the administration of 3-hydroxybenzylhydrazine (100 mg/kg, i.p.), a centrally active inhibitor of DOPA decarboxylase. Haloperidol (2.5 mg/kg, i.p.), a DA antagonist, markedly increased DOPA accumulation in the ST at 2 hr while a similar increase in the ME was not observed until 16 hr. Estradiol benzoate (25 µg/kg/day x 3, s.c.) increased DOPA accumulation in ME but not in ST. These results are consistent with previous findings utilizing the rate of decline of DA after α-methyltyrosine to estimate DA turnover. Haloperidol and estradiol-induced increases of DOPA accumulation in ME appear to be secondary to increases in serum prolactin concentrations since they are not seen in hypophysectomized rats. These results support the proposal that tuberoinfundibular DA nerves are regulated, in part, by circulating levels of prolactin. (Supported by NIH grant NS 09174 and Fellowship NS 06026.)

THE EFFECT OF SUBSTANCE-P ON PROLACTIN CONTENT OF THE RAT ANTERIOR PITUITARY GLAND IN VITRO. Louis De Palatis* and Robert P. Fiorindo. Dept. of Physiology. The Ohio State Univ., Columbus, Oh, 43210

Anterior pituitary (AP) glands from adult male rats were excised and incubated in medium 199 alone (controls) or in medium 199 containing synthetic Substance-P (SP) (experimental). Each control incubation flask contained 2 hemipituitaries from different animals. The contralateral AP halves were used in experimental flasks. After a 4 hour incubation period, Prolactin (PRL) contents of AP's and incubation medium were measured by the analytical disc electrophoretic-densitometric method. The concentration of PRL released into the medium by AP's incubated with SP did not differ significantly from PRL released into the medium by control AP explants. However, PRL content of AP tissue incubated with SP was significantly greater ($P < .01$) than that of control AP's when expressed both as µg/gland (54.90 ± 12.3 vs. 20.6 ± 3.1) and µg/mg AP tissue (5.57 ± 0.81 vs. 2.76 ± 0.26). These data suggest that SP may cause an increase in the synthesis but not release of rat PRL by the AP gland in vitro. (Supported by the Graduate School of the Ohio State University)

UPTAKE OF BIOGENIC AMINES BY REGIONAL SYNAPTOSOMES FROM NEONATAL SHEEP BRAIN: EFFECT OF IN UTERO THYROIDECTOMY. Walter B. Essman, J. Ayromlooi, and Eric J. Essman, Queens College, C.U.N.Y., Flushing, N.Y. 11367 and Long Island Jewish-Hillside Medical Center, New Hyde Park, N.Y. 11040.

The disposition of putative neurotransmitters is altered by a reduction in thyroid function. In the present study, male fetal sheep were thyroidectomized at 63-101 days of age with a twin control sham operated during the same Ceasarean section procedure. Sets of twin sheep were delivered at term (142.8±1.93 days) and brain tissue from the cerebral cortex, hypothalamus, and cerebellar cortex was fractionated to yield EM-verified synaptosome fractions from each. The experimental sheep at delivery met all criteria for hypothyroidism (T4= 4.1±1.7µg%; TSH=57.7±25.8µIU), as compared with their twin controls (T4=9.4±1.3µg%; TSH=2.9±1.6µIU). Serotonin uptake was significantly reduced in cortical synaptosomes (3.609± 0.012 to 1.078±0.046µM/mg prot./0.5h) and hypothalamic (4.050±0.016 to 1.673±0.335µM/mg prot./0.5h) synaptosomes ($p<0.01$). Norepinephrine uptake was decreased in cortical synaptosomes (87%). Dopamine uptake was increased ($p<.01$) in synaptosomes from the hypothalamus and cerebellar cortex of cretin sheep and the synaptosomal uptake of GABA and histamine was markedly accelerated in all regions (>100%).

The data suggest that synaptosomal uptake of putative neurotransmitters may be regulated by pre- and peri-natal thyroid status.

COMPARATIVE EFFECTS OF ESTROGENS, CATECHOL ESTROGENS, AND CATECHOLAMINES ON TYROSINE HYDROXYLASE ACTIVITY IN STRIATAL AND HYPOTHALAMIC TISSUE EXTRACTS. Mark M. Foreman and John C. Porter, Depts Ob/Gyn & Physiol, Green Ctr Reprod Biol Sci, Southwestern Med Schl, Dallas, TX 75235.

Hypothalamic tissue has the capacity to oxidize estrogens to catechol estrogens, suggestive of the view that catechol metabolites of estrogens may have a role in modulating hypothalamic catecholaminergic activity. In the present studies, we compared the effects of estrogens, catechol estrogens, and catecholamines upon tyrosine hydroxylase (TH) activity in homogenates prepared from rat striatal and hypothalamic tissue. Dopamine (DA), norepinephrine (NE), 2-hydroxyestrone (2OH-E1), and 2-hydroxyestradiol (2OH-E2) were found to suppress TH activity of both striatal and hypothalamic preparations. Catechol estrogens were found to be equipotent with NE and less potent than DA in ability to suppress TH activity. Parent estrogens, estrone and 17β-estradiol, as well as the O-methylated metabolites, 2-O-methylestrone and 2-O-methylestradiol, were found to have no consistent effect. The inhibitory effects of 2OH-estrogens and catecholamines were found to be dependent upon pterin concentrations. These latter findings were suggestive of a competitive interaction between catechols and pterin, and were supported by results of further experiments in which a decrease was found in pterin binding affinity (elevated Km) in the presence of either catecholamines or 2OH-estrogens. The results of the present study are indicative that 2OH-estrogens may mediate acute neural responses to estrogens, and that these effects may be terminated by O-methylation of the catechol nucleus.

AMITRIPTYLINE-INDUCED SUPPRESSION OF GROWTH HORMONE IN ACROMEGALY. Allan R. Glass, Marcus Schaaf, and Richard C. Dimond. Kyle Metabolic Unit, Walter Reed Army Medical Center, Washington, D.C. 20012

Amitriptyline(AMI) is thought to work by inhibiting reuptake of neurotransmitters, particularly serotonin, after release into the synaptic cleft. Since output of growth hormone (GH) in acromegaly can be altered by agents, such as bromocriptine, which interact with neurotransmitter pathways, we examined whether AMI might affect GH release in acromegaly. 5 men with acromegaly resistant to surgery and radiotherapy were given AMI (100 mg daily at bedtime) for one month, and plasma GH was measured every 2 hrs for 24 hrs in each subject before and after AMI. AMI resulted in significant ($p<.05$) reduction in 24 hr mean plasma GH in 3 of the 5 subjects (fall in mean plasma GH 44%, 22%, 18%). In one of these 3 subjects, mean 24 hr plasma GH fell during 2 separate trials of AMI and remained suppressed while AMI was continued for 3 months. A rise in plasma GH during late afternoon and evening (peak at 2400 hrs), which was evident before AMI, was delayed during AMI (peak at 0400 hrs). In the 3 subjects whose plasma GH suppressed with AMI, the reductions in plasma GH occurred mainly in the late afternoon and evening. The plasma GH response to oral glucose was not affected by AMI. Conclusion: In acromegaly, amitriptyline lowers mean plasma growth hormone in some subjects and delays the nocturnal rise in plasma growth hormone, perhaps through its effects on neurotransmitter pathways.

STIMULATION OF BIOASSAYABLE GROWTH HORMONE SECRETION BY THYROTROPIN RELEASING HORMONE. R.E. Grindeland, S.H. Yang*, S.E. Osborne*, and T.N. Fast*. Biomedical Research Division, NASA-Ames Research Center, Moffett Field, CA 94035

The effects of thyrotropin releasing hormone (TRH) on secretion of bioassayable (BA-GH) and immunoreactive (IR-GH) growth hormones in vivo and in vitro were investigated. Cannulae were placed in the lateral ventricles of 300 g male rats and placement tested 3 days later by injection of angiotensin II (1 ug); rats showing prompt drinking responses were used 24 hours later. Saline (10 µl) or TRH (6 µg) was injected into the ventricles (IVT) of conscious rats, which were decapitated 2, 5, or 30 minutes later. Plasma IR-GH concentrations did not differ between control and TRH groups at any of the times (e.g. 30 minute control: 8.8 ± 0.5; TRH: 7.1 ± 1.9 mµg/ml) ($p>0.05$). Pituitaries of rats sacrified 30 minutes after TRH sustained 55% (48-62%: 95% C.L.) (160 µg) depletion of their BA-GH. Propranalol (10 µg), which had no effect on BA-GH or IR-GH by itself, inhibited BA-GH depletion by 80% when given IVT 8 minutes prior to TRH; it did not alter plasma IR-GH levels. Media (Dulbecco) from incubated pituitary halves showed increases in BA-GH of 70, 160, and 334% over controls in response to 100, 400, and 1600 mµg TRH; these doses of TRH increased media IR-GH 0, 23, and 26%, respectively. Propranalol (100 mµg) did not inhibit TRH (100 mµg) evoked secretion of BA-GH in vitro. Conclusions: (1) TRH stimulates secretion of BA-GH in vivo and in vitro without parallel secretion of IR-GH, (2) In vivo TRH stimulation of BA-GH involves a β adrenergic mechanism.

OPIOID PEPTIDE-INDUCED INHIBITION OF THE RELEASE OF DOPAMINE INTO PITUITARY STALK BLOOD. Gary A. Gudelsky and John C. Porter, Depts Ob/Gyn & Physiol, Green Ctr for Reprod Biol Sci, Univ of Texas Southwestern Medical School, Dallas, TX 75235.

The ability of opioid peptides to increase serum prolactin concentrations is well documented. It has been suggested that the effect of opioid compounds to increase prolactin secretion might be the result of an opioid peptide-induced inhibition of the release of dopamine from tuberoinfundibular neurons into hypophysial portal blood. In the present study, this hypothesis was tested directly by measuring the concentration of dopamine in pituitary stalk blood following the intraventricular administration of [D-Ala^2]met-enkephalinamide (ENK). Pituitary stalk blood was obtained during a 1 hr period from pentobarbital-anesthetized rats. In stalk plasma of ovariectomized rats which had received ENK (100 µg/10 µl) intraventricularly, the mean concentration of dopamine was significantly lower (0.3 ng/ml) than that in vehicle-treated animals (1.2 ± 0.3 ng/ml). Dopamine concentrations in stalk plasma of ovariectomized rats injected daily with estradiol benzoate (25 µg/kg, sc) for 3 days were approximately 4.0 ng/ml and were reduced to approximately 0.2 ng/ml after the administration of ENK. Pretreatment of these animals with the opiate antagonist, naloxone (5 mg/kg, sc), completely eliminated this effect of ENK. The ability of opioid peptides to inhibit the release of dopamine into hypophysial portal blood may be the mechanism by which these compounds stimulate the secretion of prolactin from the pituitary gland.

FLUCTUATION OF ACETYLCHOLINE CONCENTRATION IN BLOOD DURING ESTROUS CYCLE. Nobuyoshi Hagino, Arvind Modak and William B. Stavinoha. UT Hlth. Sci. Ctr. at San Antonio, Texas 78284

In our housing conditions (light on at 0500 and off at 1900 hr) female rats showed an LH surge during 1800 and 2000 hr on proestrus. Neural activity which facilitates the LH surge appeared at 1400 hr on proestrus (critical period preceed to LH surge). In these cycling female rats acetylcholine (Ach) concentration in blood was determined. Blood (0.5 ml) was collected at a 1-2 week interval through jugular vein within 2 min. after rats were exposed to ether. A mass spectrometer in conjunction with gas chromatography and pyrolysis was used for mass fragmentometry analysis of extracted samples with 0.03mM butyrylcholine iodine as internal standard. Ach increased gradually during diestrus and proestrus, however, a marked transient reduction of Ach was observed at 1400 hr on proestrus (0.54 ± 0.05nM/ml). On the morning of estrus Ach was higher (1.60 ± 0.13nM/ml) than that in the morning of proestrus (1.24 ± 0.8nM/ml). Thus the cholinergic system might suppress the LH release. In order to examine this, Ach was determined in persistent estrous rats induced by continuous light. These rats showed a higher concentration of Ach (1.52 ± 0.10nM/ml). Supplementing these observations, every other day collection of blood under ether anesthesia increased Ach in blood (1.91 ± 0.19nM/ml) and blocked ovulation. These observations favor an inhibitory effect of the cholinergic system on LH secretion. (Supported by NIH Grants: NICHD HD-10071, and NIMH MH-25168).

MONOAMINE OXIDASE ACTIVITY AND SEROTONIN METABOLISM IN THE MOUSE BRAIN. Terence R. Hall* and Hector R. Figueroa* (SPON. Elliot A. Stein). Department of Biology, Marquette University, Milwaukee, WI 53233.

Monoamine oxidase (MAO) is involved in the metabolism of serotonin (5HT), as well as other brain monoamines. MAO in the mouse brain has not been characterized. Brains from white male, 6-month-old mice were homogenized in 20 mls of 0.2M phosphate buffer. Incubations were performed in buffer containing kynuramine (K) and MAO activity expressed as the amount of product (4-hydroxyquinoline, 4HQ) formed as measured fluorometrically. Maximal enzyme activity was found at pH 9.0. Production of 4HQ was linear with respect to dose of homogenate. The Q_{10} for the reaction was 2.1. Dopamine, norepinephrine and 5HT, but not histamine, lysine and glutamine, inhibited production of 4HQ. Both pargyline (P), a specific MAO inhibitor, and 5HT competitively inhibited conversion of K to 4HQ. In vivo, MAO activity was reduced 97% within 0.5 h after P injection. Brain 5HT content after P was time-dependent. Inhibition of MAO was related to the dose of P administered, as was brain 5HT accumulation. Pituitary prolactin content increased after P administration. These results show: (1) the optimal conditions for mouse brain MAO assay, (2) that MAO is important in regulating 5HT, (3) that inhibition of MAO by pargyline is a useful method for calculating 5HT turnover index. (Supported by a grant from MU Committee on Research)

DIURNAL VARIATION IN NALOXONE EXCITATION OF DORSAL HORN UNITS IN THE SPINAL CAT. James L. Henry, Department of Research in Anaesthesia, McGill Univ., Montréal, P.Q., H3G 1Y6.

Earlier, it was found that i.v. administration of naloxone to the anaesthetised spinal cat excites dorsal horn nociceptive neurones without affecting neurones responding only to innocuous stimuli. Other evidence that pain thresholds and that plasma levels of beta-lipotropin follow diurnal variations suggests that central nociceptive pathways may be influenced by circulating opioid peptides, likely of pituitary origin. To investigate this possibility, the earlier experiments were repeated at night and during the day. In chloralosed cats the spinal cords were transected at L_1 and segments L_5-L_7 were exposed for recording. Extracellular unit spikes were recorded with glass micropipettes filled with 2.7 M NaCl. Single units responding in a reproducible way to periodic applications of noxious radiant heat were tested. Naloxone (0.1-0.4 mg/kg i.v.) increased the on-going discharge rate of all units tested during the day. This response began within one minute, reached its maximum at 3-5 min and persisted for more than one hour. Naloxone also facilitated the response of these neurones to noxious heat. In similar experiments at night naloxone failed to alter the discharge rates or the nociceptive responses of any neurones. These observations suggest that an endogenous opioid acts on a substrate in the spinal cord to reduce transmission in pain pathways, and that the levels of this opioid follow a diurnal variation, suggesting a possible pituitary origin.
(Supported by the Canadian MRC and the Québec MRC)

EFFECT OF BROMOCRIPTINE TREATMENT ON PLASMA LH CONCENTRATIONS IN OVARIECTOMIZED EWES. T. G. Hill*, C. W. Allis ton and P. V. Malven. Purdue University, W. Lafayette, IN 47907.

Twelve ovariectomized ewes were exposed to 3-day trials in which ambient temperature/humidity conditions produced rectal temperatures indicative of normo- or hyperthermia. In 24 of 48 trials, ewes received twice daily sc injections of 1 mg of the dopamine agonist, bromocriptine (CB-154), beginning at 1900 hr on day 1. Plasma LH was measured at 10-min intervals for 4 hr on days 2 and 3. Statistical analyses included (1) comparison of means with the Newman-Kuels' test and (2) rhythmicity analysis of episodic profiles of plasma LH during each 4-hr sampling. Bromocriptine treatment of normothermic ewes decreased mean LH (11.0 vs 6.5 ng/ml, $P < .001$) and also tended to reduce LH rhythmicity ($P < .10$). Hyperthermia alone decreased mean LH (11.0 vs 8.2 ng/ml, $P < .01$) but had no effect on LH rhythmicity. Since mean LH was already inhibited in hyperthermic ewes, bromocriptine treatment did not decrease mean LH any further (8.2 vs 6.6 ng/ml, $P > .05$), but it did decrease LH rhythmicity ($P < .01$). It should be noted that mean LH was the same for normothermic ewes receiving agonist (6.5 ng/ml) as for hyperthermic ewes receiving it (6.6 ng/ml). In summary, either hyperthermia or dopamine agonist can inhibit mean LH in ovariectomized ewes, but the agonist tends to have a greater effect. Prolactin (PRL) was also measured in all plasma samples, and hyperthermia increased mean PRL while dopamine agonist decreased it.

EFFECT OF AMINEPTINE ON HYPOTHALAMIC CATECHOLAMINE TURNOVER AND SERUM PROLACTIN RELEASE IN MALE RATS. Charles A. Hodson, Richard W. Steger, Dean Van Vugt* and Joseph Meites. Neuroendocrine Research Laboratory, Dept. of Physiology, Michigan State Univ., East Lansing, MI 48823

The effect of amineptine (AM), an inhibitor of dopamine (DA) reuptake, on prolactin (PRL) release and hypothalamic catecholamine content and turnover was studied in male Sprague Dawley rats. Amineptine at doses of 1, 10, 25, 50, and 100 mg/kg (IP in 0.87% NaCl) significantly reduced PRL levels in rats killed by decapitation 1 h after injection ($P<0.01$). At 25 mg/kg, AM treatment reduced serum PRL significantly between 15 minutes and 2 h post injection, by 4 h post injection serum PRL had returned preinjection values. PRL release by pituitary halves in culture was not altered by AM at concentrations of 10, 100 or 1000 ng/ml of media. Anterior hypothalamus (AH) and medial basal hypothalamus (MBH) DA and norepinephrine (NE) content was not altered 30, 60 or 90 minutes after injection of 20 mg AM/kg bw. AM at 20 mg/kg bw however, enhanced DA but not NE depletion by 250 mg alpha-methyl-para-tyrosine (AMPT)/kg bw in the AH DA depletion in the AH 1 h after drug injection was 54% in the AMPT treated controls and 67% in the AM and AMPT treated rats ($P<.05$). These results suggest that AM reduced PRL release in the male rat by increasing hypothalamic DA turnover but has no direct effect on PRL release at the pituitary level.
(Supported in part by USPHS. NIH Grant AM 047-84)

HYPOTHALAMIC NOREPINEPHRINE AND DOPAMINE TURNOVER IN OVARIECTOMIZED OLD RATS TREATED WITH GONADAL STEROIDS, H.H. Huang*, J. Simpkins* and J. Meites, Physiology Depart., Michigan State University, East Lansing, MI 48824.

Steady state concentration and turnover of NE and DA were measured in the anterior (AH) and posterior hypothalamus (PH) of 20-22 mo old and 4-5 mo old ovariectomized rats treated with estrogen or with estrogen followed by progesterone. In old rats, concentration and turnover of NE were significantly lower in the AH as compared with corresponding young rats, but there were no differences in DA concentration. 4 hrs after progesterone injection (critical period preceding the gonadotropin and prolactin surge), there was a decrease in DA turnover in the AH of young rats, but not in old rats. Concentration and turnover of NE and DA were not different in the PH between old and young rats, and NE and DA turnover were unaltered by a single injection of progesterone. These results provide additional evidence that loss of cycling and decreased stimulation by ovarian steroids on gonadotropin release in old rats is due largely to depressed catecholamine activity in the AH (aided in part by NIH research grants AG00416 from the National Institute on Aging and AM04784 from the National Institute for Arthritis, Metabolism and Digestive Diseases).

INHIBITION BY RAT SERUM OF PROLACTIN (PRL) PRODUCTION BY RAT ANTERIOR PITUITARY CELLS IN VITRO. W. C. Hymer and E. C. Augustine, The Pennsylvania State University, University Park, PA 16802.

We have previously shown that rat pituitary mammotrophs cultured in α-modified Eagle's medium supplemented with 20% horse serum produce PRL at a rate where intracellular stores are renewed every 9 hrs. (Wilfinger et al., Endocrinology, in press). We now report that addition of rat serum (RS, 200µl) from untreated F-344 ♀ rats greatly impaired PRL production in this assay system (53.3±1.6% of controls). This response was dose-related and developed progressively with time (3 days) in culture. When RS was present only during the first 3 days of a 9 day period, PRL production rose to control levels. Mammotrophs may lose responsiveness to RS after a prolonged culture period. The inhibitory effect of RS was reduced 45-76% (3 exps.) by heating (56° C, 1 hr.). Dialysis for 24 hrs at 4° C against 0.85% NaCl did not alter inhibitory activity. Porcine, newborn and fetal calf, rabbit, guinea pig and human serum were comparable to RS. However, calf and Rhesus monkey serum had minimal activity. Preliminary experiments intended to determine how the endocrine status of the serum donor may affect activity have shown thus far that a) ovariectomy had no effect, b) estrogen pretreatment slightly decreased the inhibition, c) sex of the donor had no effect, and d) hypophysectomy slightly decreased activity. Taken together these results implicate the presence of a potent PIF in rat serum.

TUBEROINFUNDIBULAR DOPAMINERGIC (TI-DA) NERVE ACTIVITY DURING THE ESTROUS CYCLE OF THE RAT. C.A. Johnston*, K.T. Demarest* and K.E. Moore, (Spon: G.D. Reigle). Dept. of Pharmacology and Toxicology, Mich. State Univ., E. Lansing, MI 48824.

There are conflicting reports on changes in activity of TI-DA neurons during the estrous cycle. In the present study TI-DA neuronal activity was estimated using the accumulation of DOPA after the administration of a decarboxylase inhibitor. No changes in DOPA accumulation in the median eminence (ME), striatum (ST) or neurointermediate lobe (NIL) were observed on the morning of diestrus, metestrus or proestrus. DOPA accumulation in the ME increased in the late evening of proestrus and the morning of estrus. Smaller but temporally related changes were also noted in the ST and NIL.

DOPA ACCUMULATION (ng DOPA/mg protein)

Area	Proestrus				Estrus	
	800h	1200h	1800h	2400h	800h	1200h
ME	16.4	17.9	17.7	21.6	26.8	26.9
ST	9.6	11.5	11.9	2.6	12.9	9.2
NIL	0.8	0.9	0.9	1.0	1.2	1.0

The increased accumulation of DOPA in the ME occurred 6-14 hr after the proestrus surge of prolactin. This delay in the activation of the TI-DA nerves is consistent with previous studies in which serum prolactin concentrations were elevated by pharmacological means. These results suggest that the proestrous surge of prolactin is not the result of a reduction in the tonic inhibitory action of TI-DA neurons.
(Supported by NIH grant NS 09174 and Fellowship NS 06026.)

ROLE OF CENTRAL NEUROTRANSMITTERS IN THE ACTION OF MORPHINE (M) ON THE SECRETION OF PROLACTIN (PRL), GROWTH HORMONE (GH) AND THYROTROPIN (TSH). J.I. Koenig*, M.A. Mayfield* and L. Krulich. Dept of Physiology, UTHSCD, Dallas, TX 75235

Unanesthetized, adult male rats with permanent indwelling right atrial cannulae were used in most instances. Blood samples were taken at 0, 10, 30 and 60 min after an i.v. bolus of M (3 mg/kg). Plasma PRL and GH were significantly elevated while TSH was depressed. Pretreatment with 0.6 mg/kg naloxone (NAL) blocked the elevation of PRL due to M while failing to antagonize either the elevation in GH or the depression of TSH, however 6.0 mg/kg NAL blocked the M induced rise of GH. Interruption of central serotonergic transmission by metergoline (1 mg/kg), PCPA (250 mg/kg, 72 hrs before use) or 5, 7-dihydroxytryptamine (250 µg, intraventricular) antagonized the PRL response due to M without affecting the GH response, however metergoline antagonized the depression of TSH. Depletion of norepinephrine with DDC (400 mg/kg) abolished the elevation of GH due to M without affecting the PRL response. Blockade of dopamine receptors with spiroperidol (0.1 and 0.01 mg/kg) failed to alter any of the M induced hormone changes. In conclusion, our results indicate that stimulation of PRL secretion by M involves activation of the central serotonergic system but not inhibition of the dopaminergic system. The serotonergic system may also be instrumental in the inhibitory effect on TSH secretion, whereas noradrenergic mechanisms seem to mediate the activation of GH secretion. Supported by NIH Grants #HD07062 and #HD09988.

TEMPORAL EFFECTS OF TRH AND SEROTONIN (5-HT) ON SIZE HETEROGENEITY OF PLASMA PROLACTIN IN OVARIECTOMIZED, POLYESTRADIOL PHOSPHATE-TREATED (OVX+PEP) RATS. David M. Lawson, Dept. Physiol, Wayne State Univ. Sch. of Med., Detroit, MI. 48201.

Blood was drawn from OVX+PEP rats by aortic catheters at 2, 5,10,15 and 25 or 2,5,10 and 25 min. after intraarterial admin. of TRH (1µg/rat) or 5-HT (10mg/kg b.w.) respectively. Plasma was pooled from 8-16 rats at each time period and eluted from Sephadex G-100 columns (2.6 x 95 cm) using phosphate-buffered saline (0.15M, pH 7.6) made 0.1% in bovine serum albumin. Prolactin was determined in each fraction eluted between the void and total volumes of the column by RIA. Plasma prolactin levels ($\bar{X}$±SEM) and % total activity in each molecular form are shown below:

	TRH					5-HT				
	Min. After Treatment									
	0	2	5	10	15	25	0	2	5	10	25
Prolactin (ng/ml)	35 ±2	326 ±27	328 ±28	263 ±29	169 ±28	93 ±21	26 ±6	383 ±91	443 ±80	329 ±81	245 ±84
Molecular Forms	% Total Activity										
"Void Vol"	- 8,6	4,0	9.4	0	14,1	-	0	3.4	5.2	0
"Big-Big"	- 4,2	0	3,3	0	8,2	-	0	0	0	0
"Big"	- 9,1	12,1	8,9	7,2	18.1	-	2.3	0	5.2	0
"Little"	- 78,1	83,1	78,5	92,8	59,6	-	97,7	96.6	89.6	100

The differences in the pattern of prolactin heterogeneity when plasma levels are similar suggest different release mechanisms following TRH and 5-HT.

GABA MODULIN: AN ENDOGENOUS PROTEIN WHICH CONTROLS GABA RECEPTOR FUNCTION AND MEMBRANE PHOSPHORYLATION. A. Leon*, A. Guidotti* and E. Costa. Lab. Preclin. Pharmacol. NIMH, St. Elizabeths Hosp., Washington, D.C. 20032

A thermostable, acidic (MW ~15,000 dalton) protein was isolated from brain and anterior pituitary membranes. Since this protein inhibits the high affinity binding of GABA to crude mitochondrial membranes prepared from A. pituitary and other brain areas, it was termed "GABA modulin". Partially purified preparations of this protein also block, competitively with protein substrates, various types of protein kinase. These data suggest that the two inhibitory activities are related. "GABA modulin" has been purified at 4500 fold with a series of procedures including gel-filtration on Sephadex G-50, ion exchange chromatography on Dowex 50 x 8 H^+, polyacrylamide preparative gel electrophoresis. The potency of "GABA modulin" to inhibit GABA binding and cGMP-dependent protein kinase activity was maintained at a constant ratio throughout the purification procedure and the two inhibitory activities were extracted from the same protein band of SDS polyacrylamide gel electrophoresis. The content of "GABA modulin" in crude membrane preparations was greatly reduced by freezing, thawing and repeated washings with Triton X-100. In these membranes the ^{3}H-GABA binding capacity and phosphorylation activity was increased. This increase was reduced after recombination experiments with purified "GABA modulin". The results suggest that "GABA modulin" controls GABA receptor function through phosphorylation of membrane protein constituents.

MECHANISMS BY WHICH ADRENALECTOMY INCREASES PROLACTIN RELEASE F.C. Leung*, H.T. Chen*, S.J. Verkaik*, R.W. Steger, G.A. Campbell* and J. Meites, Physiology Department, Michigan State University, East Lansing, MI 48824.

The mechanisms responsible for the rise of prolactin (PRL) after adrenalectomy are unknown. Hypothalamic dopamine (DA) is known to decrease whereas serotonin (5-HT) increases PRL release. Male Sprague Dawley rats (200-225 g) were adrenalectomized (ADX) and 2-3 wks later, DA and norepinephrine concentrations in the medial basal hypothalamus (MBH) were found not to be different from intact rats; dopamine turnover (TO) also was not altered in the median eminence. Serotonin TO was significantly decreased in the MBH, but no change was found in the anterior hypothalamus. The dopamin ergic agonist, L-dopa, and antagonist, pimozide, showed similar effects on PRL release in both ADX and intact rats. The possible direct effect of corticosterone on pituitary PRL release also was examined in an 8 hr incubation system. Corticosterone at either 0.1 or 1 µg/ml medium had no effect on PRL release, but corticosterone at 10 µg/ml (basal serum level) produced a significant inhibition of PRL release. LH, TSH, and FSH release were not affected by similar doses of corticosterone indicating its action on PRL release was specific at the dose used. These results suggest that the rise of serum PRL after ADX could be due to removal of a direct inhibitory action of corticosterone on pituitary PRL release (aided in part by NIH grants AM04784, CA10771 and AM6034).

Evidence for Opiate Moderation of Hypothalamic Dopamine and its Influence on Prolactin Synthesis and Release. I.S. Login, I. Nagy and R. M. MacLeod, Depts. of Neurology and Medicine, Univ. of Virginia Sch. Med., Charlottesville, VA.

Endogenous and exogenous opiates are capable of increasing serum prolactin. Dopamine is inhibitory on prolactin secretion. We have studied the influence of the opiates on the dopaminergic system and prolactin secretion. Morphine, 60 mg/kg increased serum PRL 1700% thirty minutes after ip injection. In vitro, 13 µM morphine, Ala^2-Met^5-Enk or Met^5-Enk had no direct effect on ^{3}H-PRL synthesis or release nor did they reverse the dopamine-mediated inhibition of PRL secretion. In rats bearing prolactin-secreting transplanted tumors the synthesis and release of prolactin by the hosts' pituitary gland is greatly suppressed. These rats were implanted with osmotic pumps, sc, containing morphine or haloperidol and received 1.44 mg or 0.11 mg respectively daily for 4 days. Each treatment significantly increased the in vitro synthesis and release of ^{3}H-PRL and RIA-PRL. Hypothalamic dopamine turnover in these tumor-bearing rats is increased. In these hyperprolactinemic rats, haloperidol nullifies the enhanced dopamine turnover by blocking the action of dopamine in the pituitary gland. In contrast the opiate derivatives oppose the increased dopamine turnover in the hypothalamus. We speculate that the opiates inhibit the release of dopamine and subsequently reduce dopamine turnover which is reflected in the pituitary by an enhanced synthesis and secretion of prolactin.

NEUROCHEMICAL AND BEHAVIORAL CORRELATES OF TYPE A AND B MAO INHIBITION. V.N. Luine, V.P. Babcock, C. Paden and B.S. McEwen. The Rockefeller University, New York, NY 10021.

The ability of various Monoamine oxidase (MAO) inhibitors to antagonize estrogen-progesterone dependent lordosis responding in female rats was correlated with the extent of their inhibition of Type A and B MAO in the preoptic-hypothalamic area of the brain. Drugs were used which inhibit both forms of the enzyme (Pargyline) or which selectively inhibit either the A form (Clorgyline, Lily 51641) or the B form (Deprenyl, Harmaline + Pargyline). Significant behavioral inhibition occurred when both forms of the enzyme were inhibited by at least 85%. Selective inhibition of either the A or the B form alone by 85% was not effective in blocking lordosis responding. However, when A and B inhibitors were given simultaneously, lordosis responding was inhibited. The levels of several monoamines are increased when MAO is inhibited, and one of them, serotonin, has been postulated to exert inhibitory effects on the lordosis response. In females which showed complete behavioral inhibition, levels of this amine were raised approximately threefold in the preoptic-hypothalamic area, while smaller increases were found in animals showing lesser degrees of behavioral inhibition. (Supported by PHS grants HD12011 and NS0708 and grant RF0095 from the Rockefeller Foundation).

MELATONIN INHIBITS THE IN VIVO PITUITARY RESPONSE TO LH-RELEASING HORMONE IN NEONATAL RATS. Jeanne E. Martin and Scott McKellar*. Washington Univ. Med. Sch., St. Louis, MO

The effects of melatonin (MEL) on the in vivo pituitary LH response to LH-releasing hormone (LHRH) were examined in neonatal male and female rats, adult male rats, and adult male animals either pinealectomized (PX) or maintained in constant light (LL) for at least 3 weeks. Animals were given saline or MEL (1-100 µg/rat) followed by saline or LHRH (10-1000 ng/rat) at separate sc sites. Blood was collected without prior injection or 15, 30, 45, or 60 min afterwards; serum LH was measured by RIA. In neonatal male and female rats, 1 µg MEL significantly suppressed by 65% LH release by LHRH at 15 min. Suppression was maintained for at least 60 min, which indicates that MEL blocks rather than delays the response to LHRH. By contrast, in normal, PX, and LL male rats, 100 µg MEL had no detectable effect on either the magnitude or time-course of LH release by LHRH. These data extend our previous in vitro findings by demonstrating that MEL is a potent inhibitor of the pituitary response to LHRH in intact neonatal rats but not in adult animals. Reduction of endogenous MEL levels in adult rats by pinealectomy or constant light does not restore neonatal pituitary responsiveness to the pineal indole. Factors responsible for the developmental loss of MEL inhibition of LHRH-induced LH release and the role of this inhibition in reproductive maturation remain to be determined. (Supported by the Population Council.)

HYPOTHALAMIC TYROSINE HYDROXYLASE ACTIVITY AND PLASMA PROLACTIN AND LUTEINIZING HORMONE LEVELS IN THE DEVELOPING RAT. P.J. Murphy* and A.E. Jimenez* (SPON: Donald C. Meyer). Univ of Louisville, School of Medicine, Louisville, Ky. 40201

The purpose of this experiment was to determine the relationship between hypothalamic tyrosine hydroxylase (TH) activity and plasma prolactin (PRL) and luteinizing hormone (LH) levels during sexual maturation. Male and female rats were killed by decapitation at 10,20,30,40 or 50 days of age. PRL levels were basal in 10 and 20 day old females. A significant increase in PRL levels occurred in 30 day old females compared to 10 and 20 day old females, which was followed by a decrease in PRL at 40 days. The highest PRL concentration was observed in the 50 day old adult females. PRL concentrations in males were similar to those of females from 10-40 days. In the 50 day old adult male rat, PRL concentration was significantly decreased compared to the 30 day value. LH levels were basal in most male and female rats. In female rats, there was a significant increase in hypothalamic TH activity from 10 to 20 days and from 20 to 30 days followed by a decrease at 40 and 50 days. Similar results were found in 10-50 day old male rats. These results suggest that TH activity in the hypothalamus of the rat increases with age up to 30 days and that this increase is related to the increase in PRL prior to puberty. Also, hypothalamic TH activity is constant from age of onset of puberty to mature adult. Diurnal and cyclic changes in hypothalamic TH activity in adult cannot be excluded.

PULSATILE LH PATTERNS IN OVARIECTOMIZED (OVX) RATS: INVOLVEMENT OF NOREPINEPHRINE AND DOPAMINE IN THE RELEASE OF LHRH AND LH. A. Negro-Vilar, J.P. Advis*, S.R. Ojeda and S.M. McCann, Univ TX Hlth Sci Ctr, Dallas, TX 75235

Cannulated OVX rats were bled every 10 min. for 2 hr. to characterize their individual patterns of LH release. After the last sample, all rats were decapitated and their brains removed for analysis of LHRH, norepinephrine (NE) and dopamine (DA) levels in median eminence (ME), arcuate-ventromedial (A-VM) and suprachiasmatic-medial preoptic region (Sch-PO), to determine if changes in NE, DA and LHRH levels in any of those areas could be observed at different points during the pulsatile release of LH. The results showed that when LH levels started to increase, NE levels peaked in the Sch-PO, whereas a sharp drop in DA and LHRH levels in the ME was detected, which may reflect an acute release in the ME of both DA and LHRH. When LH levels reached peak values, NE levels in Sch-PO returned to lower values, and DA and LHRH in the ME rose to higher levels. Inhibition of NE synthesis with diethyldithiocarbamate (DDC) resulted in suppression of LH pulses. L-dopa administered after DDC induced an increased release of LH both in OVX and in OVX-estrogen-primed rats with a simultaneous inhibition of PRL release. Peak levels of LH after L-dopa coincided with increased DA levels in ME, no change in NE and a clear drop in LHRH. The results suggest that both NE and DA are involved in the pulsatile release of LH in OVX rats. Supported by NIH Grant HD-09988 and the Ford Foundation.

DIURETIC ACTION OF CLONIDINE IN THE RAT. Myron Miller. VA Med. Ctr. & SUNY, Upstate Med. Ctr., Syracuse, NY 13210.

The CNS regulation of antidiuretic hormone (ADH) may be at least in part under adrenergic control (beta adrenergic stimulatory, alpha adrenergic inhibitory). Clonidine, an alpha adrenergic agonist which can cause a diuresis in experimental animals, was studied in Brattleboro rats heterozygous for hereditary hypothalamic diabetes insipidus (DI) to determine if the induced diuresis could be due to inhibition of ADH release. Rats given s.q. clonidine in doses of 50-300 µg/kg body wt exhibited a prompt dose-related diuresis. 100 µg/kg body wt caused urine volume to increase from 0.2±0.1 (SEM) to 4.0±0.5 ml/hr while urine osmolality decreased from 1603±137 to 333±56 mOsm/kg. The diuresis was not accompanied by an increase in water intake. Continuous delivery of drug by s.q. osmotic pump at a rate of 5 µg/hr demonstrated that the diuretic effect was transient and could not be maintained beyond 4 hrs. In response to clonidine-induced diuresis, plasma osmolality increased from 301±1 to 310±1 mOsm/kg and plasma ADH measured by RIA rose from 5.1±0.9 to 21.6±7.2 µU/ml at 60 min after drug administration and urinary ADH rose from 19.6±3.7 to 48.6±5.3 µU/hr. Clonidine increased urinary excretion of creatinine, sodium, potassium and total solute. Clonidine diminished the antidiuretic action of ADH administered to Brattleboro rats homozygous for DI. Thus, clonidine-induced diuresis appears due not to alpha adrenergic inhibition of ADH release but rather to hemodynamic actions with resultant sodium and solute diuresis.

APPARENT ASSOCIATION OF DOPAMINE WITH THE PROLACTIN SECRETORY GRANULE. D. Dale Nansel, Gary A. Gudelsky, and John C. Porter, Depts of Ob/Gyn & Physiol, Green Ctr for Reprod Biol Sci, Southwestern Medical School, Dallas, TX 75235.

The subcellular compartmentalization of dopamine in the anterior pituitary gland of the rat was investigated utilizing continuous sucrose density gradient centrifugation. Two sets of dopamine-containing subcellular particles could be distinguished in anterior lobe homogenates. One of the sets contained particles which, on the basis of their comparatively low buoyant densities, could have been of cellular membrane origin. The other set was comprised of much denser particles. Furthermore, this set of dense dopamine-containing particles could not be distinguished from the set of particles, i.e., secretory granules, which contained prolactin. The amount of dopamine associated with these prolactin-containing particles was markedly increased in pituitary glands from rats which were injected with L-DOPA. This effect was eliminated when rats had been treated with bromocriptine. Anterior pituitary glands, after incubation with 10^{-4} M dopamine, contained an increased amount of dopamine associated with prolactin-containing particles. This apparent uptake of dopamine was attenuated when the pituitary glands were preincubated with the dopamine agonist, lergotrile (10^{-4} M). Thus, it appears that dopamine can become associated with prolactin secretory granules and that the amount of dopamine associated with these granules is influenced by the availability of dopamine and/or its receptors. It is interesting to speculate that this apparent association of dopamine with prolactin secretory granules may be involved in the regulation of prolactin secretion.

ON THE HYPOTHALAMIC MECHANISM BY WHICH PROSTAGLANDIN E_2 STIMULATES GROWTH HORMONE (GH) RELEASE: IN VIVO AND IN VITRO STUDIES. S.R. Ojeda, A. Negro-Vilar and S.M. McCann, Dept. Physiol,, UTHSC, Dallas, TX 75235

To determine if the stimulatory effect that prostaglandin E_2 (PGE_2) exerts on pituitary GH release by acting on the hypothalamus is mediated by an inhibition of somatostatin (SRIF) secretion, several experiments were conducted. In vivo treatment of male rats with indomethacin (Id) or in vitro administration of the drug to suppress prostaglandin (PG) synthesis induced a transient increase in basal in vitro release of SRIF by median eminence (ME) fragments. Incubation of MEs with different concentrations of PGE_2 or $PGF_{2\alpha}$ did not depress SRIF release. Nevertheless, PGE_2 inhibited the stimulatory effect of dopamine (DA) on SRIF release by the ME. In vitro Id failed to facilitate the stimulatory effect of dopamine (DA) on SRIF release by the ME. However, if ME fragments were incubated with PGE_2 in the presence of Id, an inhibitory effect of the P (on the release of SRIF became apparent. Third ventricular injection of PGE_2 in male rats elevated GH levels. A prior iv injection of an anti-SRIF serum elevated basal GH levels and greatly enhanced the GH response to PGE_2. It is suggested that the effect that PGE_2 exerts on the hypothalamus to evoke GH release is primarily mediated by an enhanced secretion of a GH-releasing factor(s) and that although PGE_2 may play a role in modulating SRIF release, such a role may be of only minor importance. (Supported by NIH Grant AM-10073 and the Ford Foundation.)

REGIONAL BLOOD FLOW IN OVINE CEREBRAL AND NEUROHYPOPHYSEAL CAPILLARY BEDS. R.B. Page*, R. Brennan*, M. Hernandez, and D. Funsch*. Milton S. Hershey Medical Center of the Pennsylvania State University, Hershey, Pa. 17033

The response of the neurohypophyseal capillary bed to changes in $PaCO_2$ was measured in six adult sheep and compared with changes in cerebral capillary beds. The radioactive-labelled microsphere technique was employed. The first injection of labelled microspheres (^{141}Ce, nominal diameter 15μ) was made under conditions of normotension, normoxia and normocarbia. Thirty minutes later, the $PaCO_2$ was elevated to 60 mmHg and a second microsphere injection (^{85}Sr) made. RCBF (ml/100 gm/min ± SE) increased significantly in cerebral capillary beds with elevation of $PaCO_2$: Occipital Gray 56±3.2 → 148±11.3, Frontal Gray 46±3.0 → 146 ±12.7, Temporal Gray 39±2.6 → 132±13.4, Corpus Callosum 14 ±0.9 → 50±9.7, Optic Nerve 13±1.3 → 35±57. Neurohypophyseal blood flow was found to be more rapid than cerebral blood flow but not to significantly change with elevation of $PaCO_2$ (Median Eminence 548±105 → 531±98, Neural Lobe 319±39 → 393 ±47. Although the ovine neurohypophysis lacks neuronal cell bodies, its blood flow is 8 times that in cortical gray matter, suggesting that the rate of neurohypophyseal blood flow is related to neurosecretion rather than neurotransmission. The lack of response of neurohypophyseal blood flow to hypercarbia suggests that mechanisms for the control of neurohypophyseal blood flow differ from mechanisms which control blood flow in other cerebral capillary beds.

CHARACTERISTICS OF TUBEROINFUNDIBULAR (TI) AND NIGROSTRIATAL (NS) DOPAMINERGIC NEURONS IN AGED MALE AND FEMALE RATS. G.D. Riegle, K.T. Demarest* and K.E. Moore, Depts. of Physiology and Pharmacology, Mich. State Univ. East Lansing, MI 48824.

Current evidence suggests that an impairment of central dopamine (DA) neurons may be involved in the deterioration of hypothalamic function observed in the aged rat. In the present study the characteristics of TI and NS dopaminergic neurons were compared in mature (5 months) and aged (24 months) male and female rats of the Long-Evans strain. Aged male rats exhibited reduced serum concentrations of testosterone and LH. Aged females were non-cycling, displaying at least 10 days of leucocytic vaginal cytology. The concentration of DA was estimated in the median eminence (ME) and striatum (ST), regions containing terminals of the TI and NS dopaminergic neurons, respectively. The activity of these neurons was estimated by the accumulation of DOPA 30 min after the administration of a decarboxylase inhibitor. Aged female rats had reduced concentrations of DA and DOPA accumulation in the ME but not ST. Aged male rats had lower concentrations of DA in both ST and ME, but DOPA accumulation was reduced only in the ME. The reduced concentration of DA in brains of aged rats may reflect neuronal loss. Failure of DOPA accumulation to decline in the ST suggests that remaining NS-DA nerves maintain function by increasing their activity; a similar adaptive change does not appear to occur in TI-DA nerves. (Supported by USPHS grants PCM 77-24202 and NS 09174 and Fellowship 06026.)

PRE-EFFECTOR CELL DOPAMINERGIC MODULATION OF PANCREATIC INSULAR SECRETIONS. E. Samols, J. Stagner*and G. Weir, VA Medical Center and Depts. of Medicine, Univ. of Louisville, Louisville, Ky. and Univ. of Virginia, Richmond, Va.

In order to determine whether specific dopaminergic receptors modulate insular secretions, studies were performed using an isolated canine pancreas preparation (without duodenum) perfused with a normal glucose concentration. After propranolol both Dop (dopamine) and Apo (apomorphine) inhibited insulin (I) release (-65±3%/-62±3%, respectively) and stimulated glucagon (G) release (73±7%/53±7%). These effects were neutralized by either phentolamine + propranolol (I 12±4%, G 30±6% for Dop; I 12±4%, G -12±6% for Apo) or by dibenzyline + propranolol (I -23±2%, G -11±2% for Dop). Changes in somatostatin (S) secretion resembled those of I but were less in degree. This suggests that there are few, if any, dopaminergic receptors on islet cell surfaces. After propranolol + butaclamol the effects of Apo on I (-30±3%) and G (12±6%) were partially neutralized ($p < 0.005$) and were completely neutralized by the addition of dibenzyline to the blockade. Conclusions: 1) Dopaminergic receptors occur in the isolated pancreas, at a pre-effector cell level, presumably in ganglia 2) Stimulation of these receptors causes an inhibition of I and S, and stimulation of G release, by a postsynaptic adrenergic terminal relay; i.e. norepinephrine release at the effector cell level and 3) Dopaminergic modulation of insular secretions may be physiologically important.

PROGESTERONE-INDUCED TEMPORAL ALTERATIONS IN LHRH CONCENTRATIONS IN SEVERAL BRAIN NUCLEI: EFFECTS OF NE SYNTHESIS INHIBITOR, DIETHYLDITHIOCARBAMATE (DDC). J.W. Simpkins*, P.S. Kalra* and S.P. Kalra, Dept. Pharmaceut. Biol. and Ob/Gyn, Coll. Med., Univ. Florida, Gainesville, FL 32610.

Studies were undertaken to identify the brain nuclei which display temporal changes in LHRH concentrations following progesterone (P,5mg,day2,1000h) administration to estrogen-primed ovariectomized rats (5μg/day0,1000h). Rats were decapitated at 0, 2, 4, 6 and 8 h after P injection. The following nuclei were isolated by microdissection for subsequent LHRH analyses by RIA: nucleus preopticus medialis (NPOm), N. hypothalamicus anterior (AH), N. suprachiasmatic (NSC), area retrochiasmatica (ARC), N. arcuatus (NA) and median eminence (ME). At 4 h after P injection, the ME and NA LHRH concentrations increased 2 and 3 fold, respectively; there was no increase in serum LH and FSH at this time. At 6 h there was a precipitous drop in the ME and NA LHRH concentrations accompanied by peak serum LH and FSH levels. DDC treatment prior to P injection blocked these alterations in LHRH and serum gonadotropin. LHRH concentrations fluctuated little in NPOm or AH whereas in SCN and ARC a significant decrease was observed at 8 h. Conclusions: (i) P-induced alterations in LHRH levels are confined largely to the ME and NA, (ii) elevations in ME and NA LHRH concentrations precede the LH release; a rapid decline in LHRH levels is coincident with the serum LH surge, (iii) these dynamic changes in LHRH concentrations require an intact central NE component.

EVIDENCE THAT THE CENTRAL SEROTONINERGIC (5HT) SYSTEM DOES NOT MEDIATE CHANGES IN THE SECRETION OF PROLACTIN (P) AND TSH INDUCED BY ETHER STRESS IN THE RAT. M.K. Steele*, R.J. Coppings*, M.A. Mayfield*, and L. Krulich. Dept. of Physiology, UTHSCD, Dallas, TX 75235

Stress of repeated etherization and blood withdrawals elevated serum P and depressed serum TSH in adult male rats as did activation of central 5HT receptors with quipazine. The possible role of the central 5HT system in the P and TSH responses to this type of stress was therefore investigated. 5HT receptor blockers, metergoline (ME) and methysergide (MS), inhibited the P response, but they were effective only in doses which inhibit P secretion by activation of the DA receptors of the pituitary lactotrophs, while cyproheptadine (CYP) actually augmented the response. ME, MS or CYP had no influence on the stress-induced inhibition of TSH, although ME or CYP effectively blocked the TSH-inhibiting action of quipazine. Treatment with p-chlorophenylalanine (300 mg/kg i.p. 72 hrs beforehand) or with 5,7 dihydroxytryptamine (200 mg intraventricular), both of which caused a large decrease of hypothalamic 5HT concentration, did not alter the response of either P or TSH. However, the 5HT uptake blocker, fluoxetine, augmented the response of P and to a lesser degree of TSH. Conclusions: Although the results obtained with fluoxetine suggest that ether stress activates central 5 HT system, all the other results indicate that 5 HT system is not instrumental either in activation of prolactin secretion or inhibition of TSH release. Supported by NIH # HD 09988.

DISASSOCIATION OF LH AND FSH REGULATION IN TRANSITION PERIOD BETWEEN REGULAR CYCLES AND CONSTANT ESTRUS IN OLD FEMALE RATS R.W. Steger , H.H. Huang* and J. Meites, Physiology Depart., Michigan State University, East Lansing, MI 48824.

Old constant estrus (CE) or repeat pseudopregnant (PP) rats show no cyclic variation in gonadotropins and a reduced response to castration or to the positive feedback action of steroids. In order to clarify gonadotropin regulation in the transition period between regular cycles and CE, young (4-5 mo) regular cycling, mid-age (12-14 mo) irregular cycling (IRC), mid-age CE and old (20-22 mo) CE rats were ovariectomized (OVX) and blood was collected at 2-3 day intervals for 4 wks. Two wks later rats were given 10 μg estradiol benzoate (EB)/100 g BW, followed 3 days later by another EB (10 μg/100 g) or progesterone (0.5 mg P/100 g) injection. The post-OVX LH rise was reduced in the mid-age IRC, CE and old CE rats as compared to young controls. FSH after OVX did not differ. The 2nd injection of EB resulted in an LH surge that afternoon only in young rats. On the following afternoon, LH surges were evident in all but the old CE rats, whereas an FSH surge was seen in all animals on both afternoons. On the afternoon of P injection LH and FSH levels were increased in all rats although the increase of LH in the old CE rats was less than in the other groups. These results suggest that there are progressive, but different changes with age in control mechanisms for LH and FSH release (aided in part by NIH research grants AG05062 and AG00416 from the National Institute on Aging).

EFFECTS OF MORPHINE AND NALOXONE ON THE PHASIC RELEASE OF GONADOTROPINS, P.W. Sylvester*, H.T. Chen* and J. Meites, Physiology Dept., Mich. State Univ., East Lansing, MI 48824.

A daily diurnal surge of LH and FSH was induced in long-term ovariectomized rats by 2 injections of estradiol-benzoate (EB) (20 µg/rat sc) given 72 hrs apart. On the day following the 2nd injection, the animals were given 4 injections of morphine (5 mg/kg), naloxone (0.2 mg/kg) or 0.85% NaCl sc at 13, 15, 17, and 19 hrs. Blood was collected at 10, 17, 20 hrs on the day of treatment, and on the following day. The afternoon surge of LH was blocked in the morphine treated group, whereas the naloxone group showed a significantly greater LH peak than in saline treated controls. The next day, the morphine treated group showed a rebound LH surge, and the naloxone group showed only a slight LH surge. FSH responded similarly to these treatments. In another experiment, the 1st injection of EB was followed 72 hrs later by progesterone (2.5 mg/rat) sc at 1100 hrs. On treatment day, the LH surge was blocked in the morphine group, whereas the naloxone and control groups showed no difference in surge levels. On the 2nd day there was no LH surge in the naloxone or saline groups, believed to be due to progesterone shutting off the surge signal. However, the morphine group showed a large LH surge. These results suggest that naloxone acts like progesterone, potentiating the LH peak on the 1st day and suppressing it the next day (aided by NIH research grant AM04784 of NIAMDD).

ADRENOCORTICOTROPHIC HORMONE EFFECTS ON ^{14}C-CHOLINE ACCUMULATION BY RAT BRAIN SYNAPTOSOMES. J. W. Veals* and F. L. Strand, Schering Corp., Bloomfield, NJ and New York University, Department of Biology, Washington Square, NY

The presence of adrenocorticotrophic hormone (ACTH) in the incubation medium influenced high affinity ^{14}C-choline accumulation by synaptosomal preparations derived from whole rat brain and brain areas. ACTH (0.001-1.0 µg/ml) and norepinephrine (10^{-4}-10^{-6}M) increased the accumulation of ^{14}C-choline ($0.5x10^{-6}$M) by synaptosomes. Addition of both norepinephrine (NE) and ACTH resulted in greater apparent uptake than did separate addition of either to the medium. Similar effects were seen using synaptosomes from adrenalectomized or hypophysectomized rats. On the other hand, ACTH did not affect uptake of ^{3}H-NE, ^{3}H-dopamine, or ^{14}C-serotonin. In other studies on choline uptake, the effects of ACTH (0.1 and 1.0 µg/ml) and α-methyl-NE (10^{-6}) were studied on synaptosomes from various brain areas. ACTH had an apparent stimulatory effect (dose related) on synaptosomes from striatum, hippocampus, parietal cortex, medulla-pons, and hypothalamus; and inhibitory effects on synaptosomes from anterior thalamus-septal area and cerebellum. These results suggest that ACTH may have a direct extra-adrenal effect on central cholinergic nerve terminals.

ROLE OF SEROTONIN IN LH SECRETION. Richard F. Walker* and Paola S. Timiras. University of California, Berkeley, CA 94720

The objective of this study was to determine the role of rostral hypothalamic serotonin in the release of an ovulatory quantum of LH during proestrus. Cannulae for drug administration were implanted in the medial-preoptic/suprachiasmatic (MPOA/SCN) area in adult female rats and vaginal cycles monitored. When cycling was restored after surgery, monoamine synthesis inhibitors (diiodotyrosine, DIT, p-chlorophenylalanine, PCPA, α-methyl-p-tyrosine, AMT, or diethyldithiocarbamate, DDC) were administered prior to the day of LH release, i.e. in the afternoon of diestrus 2. Gonadotropins were measured in blood samples taken serially during proestrus after drug treatment and brain monoamines were assayed in the tissue surrounding the tip of the cannula. All drugs blocked the anticipated surge of LH in proestrus but only PCPA and DIT caused estrus to continue for at least one week after implantation. Norepinephrine (NE) levels were reduced in all treated rats, but serotonin was depressed only after PCPA and DIT treatment. Dopamine values remained unchanged. These data suggest that MPOA/SCN serotonin, in concert with NE, plays an integral role in the control of cyclic LH secretion; additionally after blockage of serotonin synthesis on diestrus 2, follicular growth and maintenance may continue for extended periods of time. (Supported by NIH grants AG00043-01A3 and 1 F32 AG05068).

INHIBITION OF STIMULUS-SECRETION COUPLING IN RAT LACTOTROPH CELLS BY D-600, MANGANESE, REMOVAL OF EXTRACELLULAR CALCIUM AND DOPAMINE. M.O. Thorner, J.T. Hackett, K. Daniel* and M. Callahan*. University of Virginia School of Medicine, Charlottesville, VA 22908

Recent studies on the anterior pituitary have demonstrated sodium and calcium dependent action potentials; thus the hypothesis that spikes are implicated in the excitatory drive to prolactin release has been proposed (Taraskevich and Douglas, 1977). To test this hypothesis we have performed studies on the role of sodium and calcium spikes on prolactin secretion from continuously perfused isolated rat anterior pituitary cells. Tetrodotoxin (10^{-6} M), the sodium channel blocking agent, was ineffective in altering basal prolactin secretion or inhibition of release by dopamine ($5x10^{-6}$M). D-600 (10 µg/ml), the blocker of regenerative calcium spikes, inhibited prolactin release to 30% of basal secretion. Similar inhibition was seen following dopamine $5x10^{-6}$ M, removal of extracellular calcium, or addition of 2 mM manganese (Mn). Dopamine is effective in inhibiting prolactin release only in the presence of normal extracellular calcium and not in the presence of D-600, Mn or removal of extracellular calcium. However, the dopamine inhibition can be antagonized by neuroleptics. These results indicate that calcium, but not sodium, channels are important in the high basal release of prolactin. It is proposed that dopamine inhibits prolactin release by decreasing calcium permeability of the cell membrane.

PLASMA PROLACTIN INCREASE INDUCED BY ELECTRICAL STIMULATION OF AMYGDALOID NUCLEUS. F. Velasco*, M. Velasco, H. Muñoz* and A. Parra. Sci. Res. Dept., Natl. Med. Ctr. IMSS, Mexico City, Mexico.

In five patients with stereotactically implanted electrodes in the basolateral area of the amygdala, as part of their evaluation for surgical treatment of uncontrollable, temporal lobe seizures, the effect of electrical stimulation on plasma levels of PRL, GH, FSH, LH and TSH was studied. Two to 3 weeks after implantation of electrodes the study was carried out in 2 consecutive days: on the first day a sham stimulation and on the second a subthreshold electrical stimulation of the amygdala (200-400 uAmp, 60/sec, 1 msec) were performed while serial blood samples were drawn for determinations by radioimmunoassay of the above mentioned hormones. Stimulation was accompanied in every patient by a significant rise in plasma PRL as compared with basal and sham stimulation levels ($P < 0.01$), whereas other pituitary hormones were not modified. The results suggest that the temporal lobe amygdala is related to the final hypothalamic pathway for control of PRL secretion.